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JANUARY 1966

Rowell responds to the 'cold' patient's comprehensive problem with the 'total therapy' concept

Colrex Compound

PHENYLEPHRINE TO RELIEVE NASAL CONGESTION with a potent vaso-constrictor that does not lead to "rebound congestion."

CHLORPHENIRAMINE TO COMBAT EXCESSIVE SECRETION without causing excessive drying of the delicate nasal mucosa.

CODEINE TO SUBDUE COUGH remains the best antitussive and appears to act synergistically with PAPAVERINE in the relief of cold symptoms—and to enhance aspirin analgesia.

ALUMINUM ASPIRIN TO REDUCE FEVER AND ACHE with less possibility of salicylate-induced gastric upset. PLUS VITAMIN C TO HELP MAINTAIN CAPILLARY INTEGRITY.

NEGLECTS NO ASPECT OF THE RESPIRATORY SYNDROME

Colrex Compound

EACH CAPSULE CONTAINS:

Codeine phosphate	16 mg.
(Warning: May be habit-forming)	
Papaverine hydrochloride	16 mg.
Aluminum aspirin	300 mg.
Phenylephrine hydrochloride	5 mg.
Chlorpheniramine maleate	2 mg.
Vitamin C	100 mg.

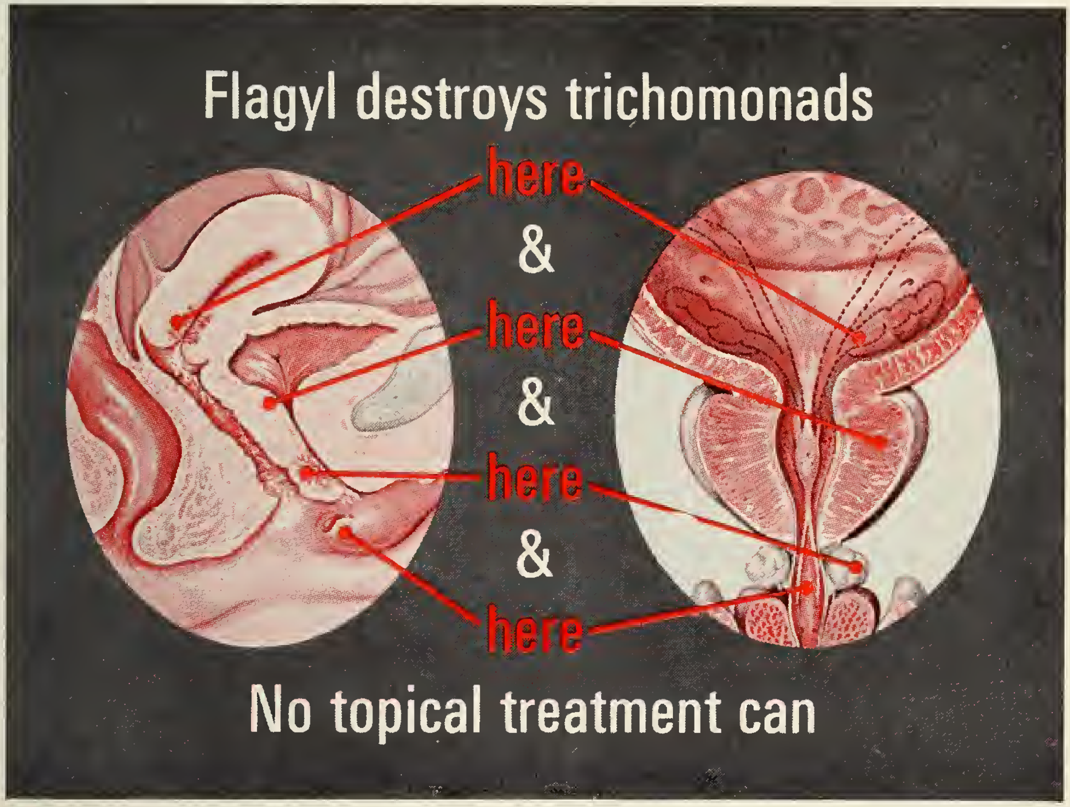
Dosage: Adults, 1 capsule 3 or 4 times daily; children, according to age and weight.

Indications: Cough, congestion, headache, discomfort and muscular aches and pains in coryza, rhinitis, sinusitis, pharyngitis, laryngitis, tracheitis, bronchitis, grippe, influenza and pneumonia.

Side effects and precautions: Side effects are infrequently encountered. Codeine and aluminum aspirin should not be given to patients with known idiosyncrasies to these drugs. Antihistaminic agents may cause drowsiness in susceptible individuals. Colrex Compound should be used with caution in hypertensive patients.

Caution: Federal law prohibits dispensing without a prescription. Class B narcotic.

ROWELL LABORATORIES, INC.
BAUDETTE, MINNESOTA



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Flagyl eliminates the difficulties and frustrations that have long attended the treatment of trichomonal infection. These difficulties arose mainly from:

1) *the failure of any previously known agent to destroy the protozoan in paravaginal crypts and glands;*
2) *the failure of any previously known agent to prevent reinfection by eradicating the disease in male consorts.*

The introduction of Flagyl removed these deficiencies. Hundreds of published investigations in thousands of patients have confirmed the ability of Flagyl to cure trichomoniasis.

Correctly used, with due attention to repeat courses of treatment for resistant, deep-seated invasion and to the presumption of reinfection from male consorts, Flagyl has repeatedly produced a cure rate of up to 100 per cent in large series of patients.

Nothing cures trichomoniasis like Flagyl.

Dosage and Administration

In *women:* one 250-mg. oral tablet t.i.d. for ten days. A vaginal insert of 500 mg. is available for local therapy when desired. When the inserts are used one vaginal insert should be placed high in the vaginal vault each day for ten days, and concurrently two oral tablets should be taken daily.

In *men:* in whom trichomonads have been demonstrated, one 250-mg. oral tablet b.i.d. for ten days.

Contraindications

Pregnancy; disease of the central nervous system; evidence or history of blood dyscrasia.

Precautions and Side Effects

Complete blood cell counts should be made before and after therapy, especially if a second course is necessary.

Infrequent and minor side effects include: nausea, unpleasant taste, furry tongue, headache, darkened urine, diarrhea, dizziness, dryness of mouth or vagina, skin rash, dysuria, depression, insomnia, edema. Elimination of trichomonads may aggravate moniliasis.

Dosage Forms

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Vaginal—500-mg. inserts

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Contraindications: Previous allergic or idiosyncratic reactions to meprobamate or meprobamate-containing drugs.

Precautions: Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of preexisting symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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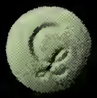

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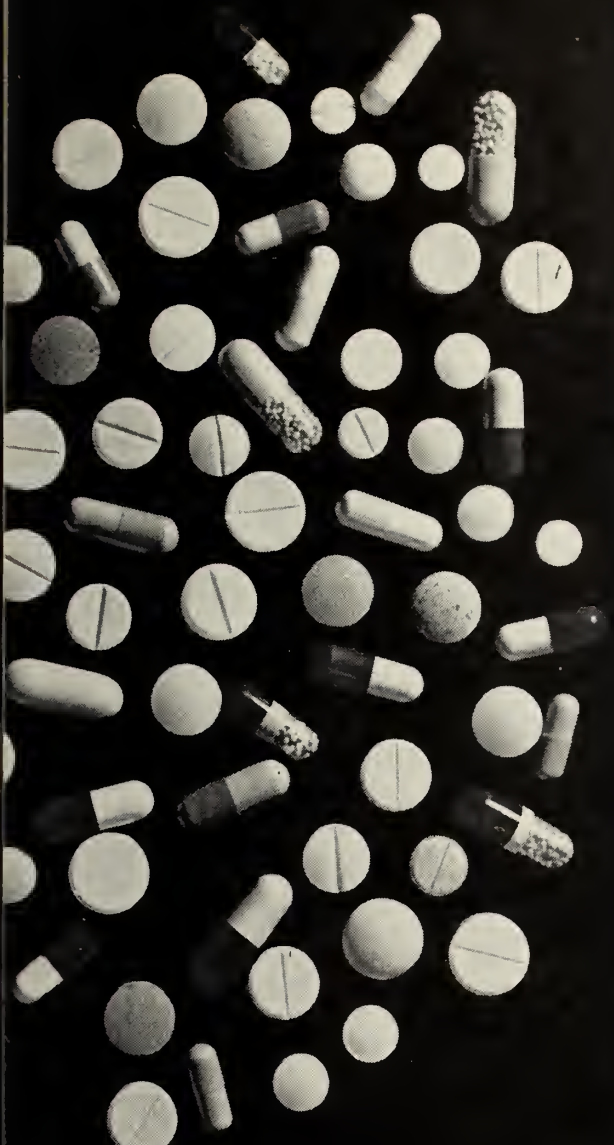

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...stimulates development of collateral circulation[4]

Side effects: Negligible—but, occasionally, transient headache may occur.

Precautions: Exercise caution in glaucoma, and with dosage forms containing phenobarbital, which may be habit forming. Full information available on request.

References: 1. Johnson, P. C., and Sevelius, G.: J.A.M.A. *173*:1231, 1960. 2. Data on file in the Medical Department, Warner-Chilcott Laboratories. Available on request. 3. Sadove, M. S.; Rosenberg, R.; Heller, F., and Shulman, M.: Am. Prof. Pharm. *31*:23, 1965. 4. Lumb, G. D., and Hardy, L. B.: Circulation (Pt. II, Cardiovascular Surgery) *27*:717, 1963.

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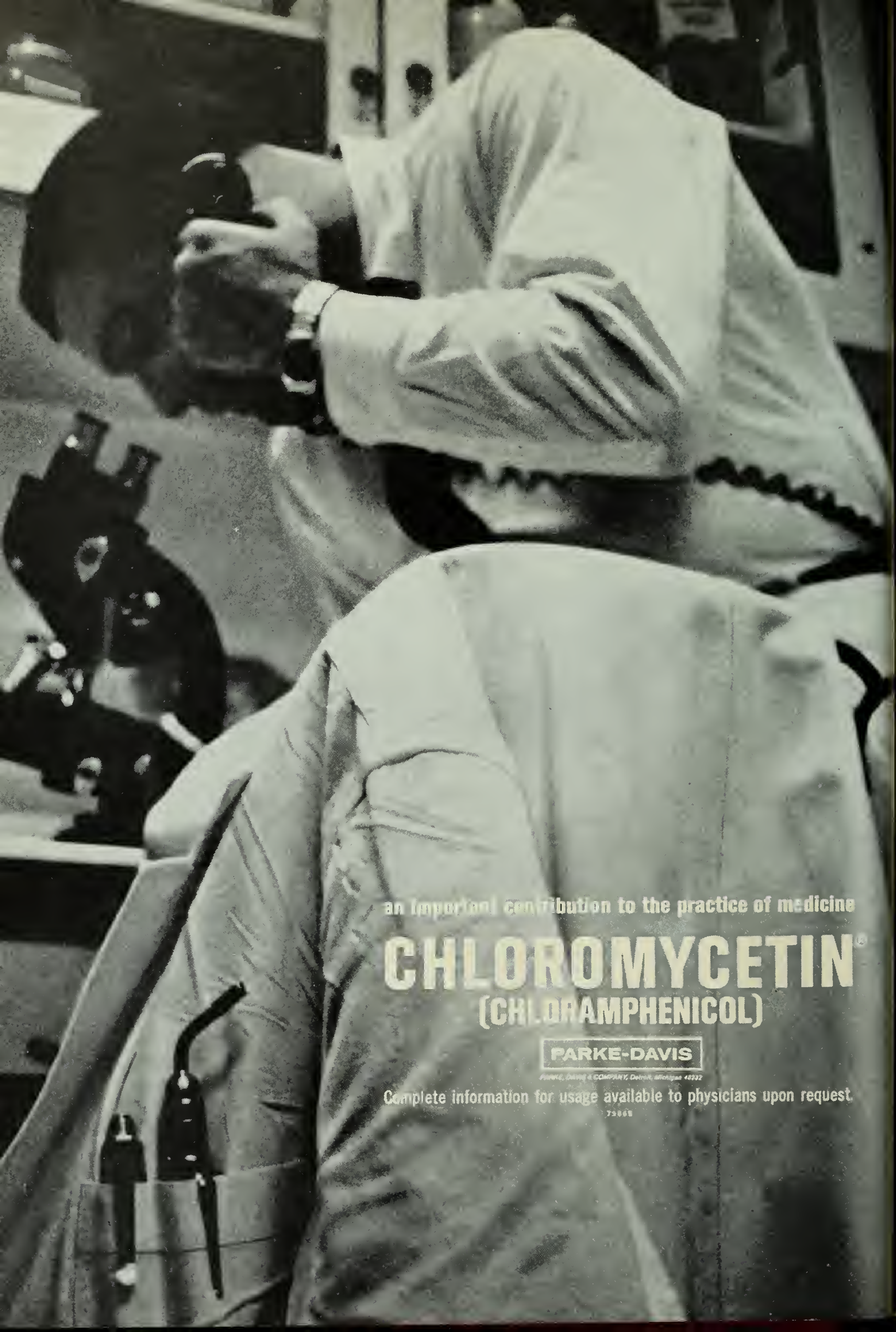

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COMING *in* *February*

Articles and features to be found in the next issue of THE JOURNAL-LANCET

The physician treating congestive heart failure is faced with a continuing diagnostic exercise and must be aware of subtle as well as overt influences that require adjustments in the therapeutic program in order to avoid disastrous complications. In their article "Some Problems in the Management of Congestive Heart Failure," Dr. Ralph R. Reed, fellow at the Mayo Graduate School of Medicine, University of Minnesota, Rochester, and Dr. Milton W. Anderson of the Mayo Clinic point out that the ingredients for satisfactory management of the usual patient are a thorough history and physical examination and experience-tempered judgment. The factors producing resistant heart failure are discussed.

Dr. Edith M. Lincoln of the Department of Pediatrics, New York University Medical Center, New York City, reviews "The Continuing Menace of Tuberculosis for Children." This article is one in the "Ruth E. Boynton Series" and deals particularly with the prevention of tuberculous infection and of complications of tuberculosis in children.

Measures taken immediately upon admission of the hemiplegic patient to the acute hospital are important to his later rehabilitation. Dr. Miland E. Knapp, clinical professor of Physical Medicine and Rehabilitation at the University of Minnesota, in his article, "Rehabilitation in Hemiplegia," advocates bed positioning and range of motion exercises even before the threat to life has subsided.

Every seriously ill asthmatic patient has a medical problem and should be so treated. Dr. Haddon M. Carryer of the Mayo Clinic states in "The Management of Acute Asthma" that more often than not asthmatic patients have other medical problems which may influence the asthma and which must be considered in the selection of therapy. Only if the entire patient, his other diseases, his emotional problems, and the ultimate effects of therapy are reviewed can the best care be given.

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Unique combination produces greater antihypertensive effect with lower doses

Eutron is the combination in a single tablet of 25 mg. Eutonyl (pargyline hydrochloride) and 5 mg. Enduron (methyclothiazide). This combination produces greater therapeutic effect than that of either component used alone. Side effects may be milder, too, as dosages are generally lower. The effective dosage is usually one tablet, once daily. Tablets are scored for greater dosage flexibility.

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Each Eutron tablet contains two proven antihypertensives in the ratio shown to be most effective in most patients.

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New **EUTRON** extends your range of treatment in moderate to severe hypertension

A single product you can use even in the presence of congestive heart failure or edema

Eight out of 10 patients respond

In clinical trials, Eutron produced normotension or a significant reduction in blood pressure in eight out of 10 patients studied. The rationale for the product is this: Eutonyl used alone is a potent antihypertensive. Its antihypertensive action is markedly enhanced by Enduron, a potassium-sparing thiazide.[1,2,3] The combination (Eutron) thus produces greater antihypertensive effect with lower dosages of the Eutonyl component, and milder side effects may be seen.

512214

1. Torosdag, S., Schvartz, N., Fletcher, L., Fertig, H., Schwartz, M. S., Quan, R. F. B., and Bryant, J. M., Pargyline Hydrochloride as an Antihypertensive Agent With and Without A Thiazide, Am. J. Cardiol., 12:822, Dec., 1963.
2. Pollack, P. J., Pargyline Hydrochloride and Methyclothiazide Combined In The Treatment of Hypertension, Cur. Thera. Res., 7:10, Jan., 1965.
3. Bryant, J. M. et al., Antihypertensive Properties of Pargyline Hydrochloride, New Non-Hydrazine Monoamine Oxidase Inhibitor Compared with Sulphonamide Diuretics, J.A.M.A., 178; 406, Oct., 1961.

BP reductions in the recumbent and sitting positions often are nearly as great as in the standing. In clinical trials, the average *recumbent* BP reduction was 36/18 mm. Hg.

The average *standing* reduction in clinical trials was 45/22 mm. Hg. Thus the difference between the standing and recumbent readings was only 9/4 mm. Hg.

Significantly lowers blood pressure in all body positions; less likelihood of orthostatic hypotension

In clinical trials, the average reduction in standing blood pressure was 45/22 mm. Hg.; in the sitting position it was 48/20 mm. Hg.; and in the recumbent position, 36/18 mm. Hg.

Because Eutron effectively reduces blood pressure in all body positions, there is reduced likelihood of orthostatic symptoms or hypotension.

This was reflected in the relatively mild character of side effects seen in clinical trials (see below).

Smooth and gradual onset

Onset of antihypertensive action is usually quite smooth. Initial reduction of systolic and diastolic readings is usually seen within a week – maximum reduction in seven to ten days.

Less troublesome side effects may be seen; frequent improvement in "sense of well-being"

Fewer than 1% of patients studied discontinued Eutron therapy because of side effects. This is due in part to the relatively low dosage needed with the combination. Usual recommended dose is one tablet daily—that is, 25 mg. Eutonyl with 5 mg. Enduron. *This is about half the usual therapeutic dose of Eutonyl given alone.* As a consequence side effects may be milder. And, as with Eutonyl given alone, the patient may well note an increased sense of well being. This is in distinct contrast to most other antihypertensive therapy.

ABBOTT

Prescribing information for **EUTRON**

INDICATIONS: Eutron (pargyline hydrochloride and methyclothiazide) is indicated in the treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. It is not recommended for use in patients with mild or labile hypertension amenable to therapy with sedatives and/or thiazide diuretics alone.

CONTRAINDICATIONS: Eutron is contraindicated in patients with pheochromocytoma, advanced renal disease, paranoid schizophrenia and hyperthyroidism. Until further experience is gained it cannot be recommended for use in patients with malignant hypertension, children (under 12 years of age), or pregnant patients.

The concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyldopa. A drug-free interval of two weeks should separate therapy and use of these agents.

WARNINGS: Pargyline hydrochloride is a monoamine oxidase inhibitor. Patients should be warned against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When it is necessary to administer alcohol, narcotics (notably meperidine), antihistamines, anesthetics, barbiturates and other hypnotics, sedatives, tranquilizers, or caffeine, these agents can be used cautiously at a dosage of ¼ to ⅕ the usual amount. Avoid parenteral administration where possible. Withdraw pargyline two weeks before elective surgery.

Patients should be warned about the possibility of postural orthostatic hypotension. Those with angina or other evidence of coronary disease should not increase physical activity. Pargyline may lower blood sugar. Potassium depletion is unlikely at the recommended dosage, but if it occurs, adjust dosage or withdraw or provide added natural food sources of potassium; potassium tablets should be avoided wherever possible, as bleeding or obstructive ulceration of the small bowel has been associated with their use; potassium levels should be especially watched if the patient is on digitalis or steroids, or if hepatic coma is impending.

PRECAUTIONS: When determining the antihypertensive effect of Eutron, blood pressure should be measured while the patient is *standing*. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Pargyline has not been shown to cause damage to body organs or systems. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. The drug should be used with caution in patients with liver dysfunction. With prolonged therapy, examine patients for change in color perception, visual fields, and fundi.

Elevated blood urea nitrogen, serum uric acid or blood sugar are possibilities attributable to the methyclothiazide in Eutron. Methyclothiazide may also reduce arterial response to pressor amines. Blood dyscrasias, including thrombocytopemia with purpura, agranulocytosis and aplastic anemia, have been seen with thiazide drugs.

SIDE EFFECTS: The use of pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extra-pyramidal symptoms have been reported. Drug fever is extremely rare. Congestive heart failure has been reported in a few patients with reduced cardiac reserve. Nocturia has been observed with the combination. If side effects persist, despite symptomatic therapy or reduction of the dose, discontinue the drug.

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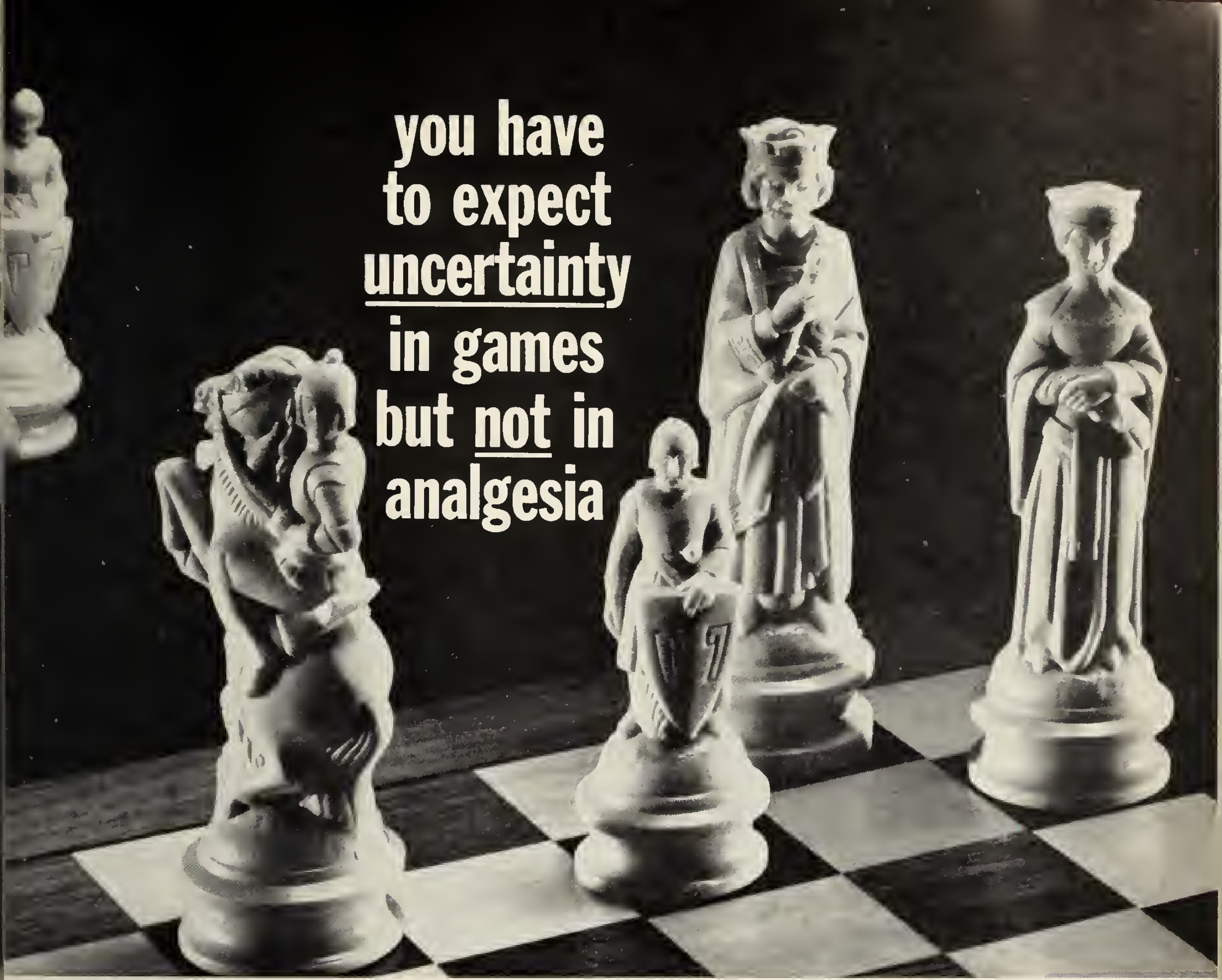

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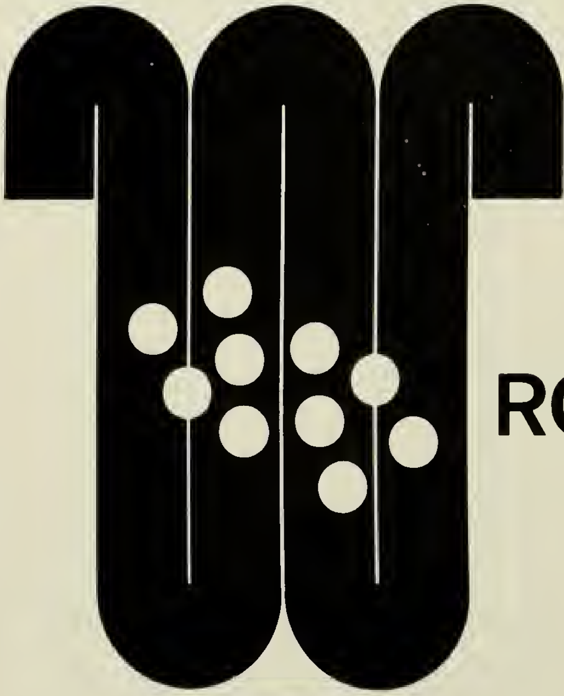

Daily dosage (6 tablets) provides . . . lipase to digest the equivalent of 21% of the average daily fat intake plus ox bile and dehydrocholic acid to further aid in fat digestion . . . amylase to digest the equivalent of 49% of the average daily starch intake . . . pepsin, trypsin and chymotrypsin to digest the equivalent of 92% of the average daily dietary protein.

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Series on NEUROLOGY *for the* PRACTITIONER

The Confused Patient

GEORGE C. FLORA, M.D., and A. B. BAKER, M.D.

Minneapolis

CONFUSIONAL STATE refers to a partial impairment of consciousness with much less impairment of motor function. It is characterized by deleria with or without hallucinations, delusions, and often restlessness and agitation. The syndrome may challenge the physician's diagnostic skills unduly if the etiological significance of intoxications is overlooked. Intoxications, both exogenous and endogenous, are the single most common cause of this disorder. Exposure to a toxin as well as other common causes of this syndrome often relates directly to the different age groups and justifies the following classification.

CAUSES IN INFANCY, CHILDHOOD, AND YOUTH

Infections. In the younger age groups infections of the middle ear, pneumonia, exanthemata, and meningitis are the most common cause of confusion. The cerebral dysfunction is frequently much more evident and alarming than is the infectious process.

On examination the temperature will be elevated and the source of infection will be found if it is searched for meticulously. The faint blush of a tympanic membrane, or the earliest Koplik spot may often clarify a puzzling clinical problem. The nuchal tone may be only suggestively increased in meningitis or in an encephalitic complication of exanthemata at the time the confused state is most prominent. The diagnosis can be established by the presence of a leukocytosis, X-ray evidence of a pneumonia, discovery of purulent exudate behind the tympanic membrane, or the discovery of an increased cerebrospinal fluid cell count.

Treatment consists of culturing the causative organism and then treating the patient with appropriate antibiotics. The exanthematous diseases, if not preventable, must be treated symptomatically.

Toxins. The accidental ingestion of sleeping pills, flavored aspirin, tranquilizers, dietary aids, and anodynes is common in this age group. The sudden development of confusion in a youngster is indication for a search of the child's environment for a source and hopefully the identification of an ingested toxin.

Examination reveals little; occasionally a suppression of all deep tendon reflexes may be found. Laboratory studies are usually not helpful. If such a condition is suspected, all unabsorbed toxin may be recovered by gastric lavage and the patient is then treated symptomatically. Recovery is spontaneous after a period of hours and complications rarely occur.

Postictal state. Confusion appearing after a convulsion may be difficult to evaluate, especially if the parents of a child are unaware of previous seizures and have failed to observe the motor component of the current episode. The duration of this confusion, twenty to sixty minutes, is often helpful in arriving at an accurate diagnosis.

Examination is often helpful. Bruises of the tongue or on the body may suggest the correct diagnosis as does evidence of involuntary mictu-

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GEORGE C. FLORA *is assistant professor, Division of Neurology, University of Minnesota Hospital, Minneapolis, and* A. B. BAKER *is professor and director, Division of Neurology, University of Minnesota Medical School, Minneapolis.*

rition. Focal neurological deficit of a cerebral type which persists transiently after the confused period, as a Todd's paralysis, or of more persisting nature, frequently suggests a focal etiology for seizures and indicates the diagnosis.

Recovery frequently occurs before treatment can be administered. After recovery adequate investigation and medicinal control of the seizures should be instituted.

Head trauma. Many children receive head injuries while alone or when with other children who fail to mention it to any adult. Once the confusion occurs the child can offer no adequate history and unless very gross evidence of injury is present, it is often omitted from the differential diagnosis.

In this age group examination should include a careful search for fresh scalp bruises, bleeding from the nose and especially from the ears. A spinal fluid examination may reveal the abnormal presence of red blood cells which is helpful diagnostically. X-ray for fractures should always be carried out if a diagnosis can not be established.

Treatment for posttraumatic confusion is symptomatic. The process is self-limiting and recovery occurs without residual effects. Those who progress to a comatose condition require more intensive observation and care and have a poorer prognosis.

CAUSES IN ADULTHOOD

Toxins. Toxins of various types are also the most common cause of a confusional state in the adult. These toxins may be due to drugs, chemicals, endogenous poison, or alcohol.

1. Acute alcoholism is the most common cause of a confusional state in this age range, but the physician seldom is called to see such cases unless secondary trauma is present. The symptom complex is characteristically that of confusion, ataxia, and dysarthria associated with loquacious injudiciousness.

Examination is of little help other than for the detection of an odor of alcohol. Laboratory tests for alcohol level in blood or in expired air are occasionally of value. The treatment for this condition is directed toward physical control of the patient to prevent secondary injury. Sedation such as intravenous amobarbital (Amytal®) is quite safe for this purpose.

2. Chronic alcoholism which is suddenly terminated for any reason—such as voluntary abstinence, hospitalization for illnesses or injuries, or acute gastroenteritis—presents a very classical confusional state known as delirium tremens. The confusional period frequently has a progressive course beginning from one to fourteen days after withdrawal of alcohol. The confusion is associated with gross tremulousness, visual and auditory hallucinations, and major motor seizures.

Examination reveals a gross rapid tremor of the extremities with markedly accentuated startle responses. Hyperhydrosis, hyperactivity, tachycardia, and dilated pupils are evident. Dental hygiene is classically poor. Hepatomegaly and small cutaneous telangiectasias over the shoulders and chest are common. The lower extremities frequently have hyperactive patellar reflexes and absent Achilles reflexes. The soles of the feet are red, cold, moist, and hypersensitive to painful stimuli. Laboratory examination is of benefit only if it substantiates a hepatocellular dysfunction —increased sulfobromophthalein (Bromsulphalein®) values—which rapidly improve during hospitalization.

Treatment is directed toward the control of hyperactivity for which paraldehyde by any feasible route is the safest. The course of the process is self-limiting, usually subsiding in three to seven days. Adequate fluid intake of 2 to 4,000 cc. daily must be maintained during the acute phase with parenteral vitamins B and C. Circulatory collapse or cardiac failure may occur in this condition and require treatment. Death occurs in 10% of delirium tremens if they are not adequately treated.

3. Barbiturate intoxication may be the cause of confusion in the adult although more commonly it presents with coma. If a history can be obtained from the patient or from secondary sources, it often reveals some emotional instability, depression, or insomnia. History from secondary sources frequently reveals a pattern of frequent, sudden, recurrent confusion which has puzzled the informants but which little concerned the patient. Examination is not helpful unless dysarthria and ataxia, rather typical "inebriation" associated with absence of ethanolic breath, are noted. Laboratory studies may be helpful in revealing elevated quantities of barbiturates in the urine or blood.

Treatment is symptomatic for these confusional states since they are both of short duration and without residual. The drug should be discontinued and less toxic ataractics administered where emotional disturbances warrant.

4. Phenothiazine intoxication produces an acute confusional state in a number of susceptible adults. A helpful history is usually available from the confused patient who complains of associated distressing vertigo and syncope. Examination is

not helpful unless a medication supply can be found on the individual or the underlying psychiatric process manifests as an obviously disordered thought or affect. The presence of dystonic movements of the head and tongue or motor restlessness and inability to sit quietly should make one suspect the use of such drugs.

Treatment is symptomatic and consists primarily of reducing the dosage or discontinuance of the drug entirely.

5. Amphetamine intoxication is quite common in patients who are on weight reduction regimens. Tolerance to these drugs is rather rapidly developed and the tendency to increase the dosage is quite common in patients intent on weight reduction. This confusional state may be associated with prominent hyperactivity and restlessness although sedative effect with somnolence may occur.

Examination may show only motor hyperactivity and tachycardia in an obese individual. Treatment may require short-term hospitalization, restraints, and sedation. The cardiac status must be protected if tachycardia is impairing output.

6. *Bromide.* Self-administration of bromides as sedatives or "nerve tonics" in the form of sodium bromide or triple bromide tablets or an anodyne such as Bromo-quinine® or Bromo-seltzer® is very common. These drugs may produce a confusional state in this age group. Neurological examination commonly shows coarse tremors of the lips and hands, an ataxic gait, dysarthria, and a severe memory defect with delusions and emotional lability. The general examination frequently reveals an aceneform rash, fetid breath, and emaciation. Laboratory confirmation may be obtained by the determination of blood and urine bromide levels.

The treatment for "bromism" is discontinuance of the exposure. The process is usually self-limiting without severe residual, although permanent psychosis is occasionally seen.

7. Intoxications from industrial toxins such as carbon monoxide, lead, arsenic and mercury, carbon tetrachloride, trichlorethylene, and carbon disulfide occur in this age range but their frequency is not great. Accidental intoxications with insecticides, weed killers and fungicides, as well as intentional poisoning with arsenic, may also rarely be a cause of confusion in this age range.

Carbon monoxide poisoning is seen in automobile mechanics working in poorly ventilated shops, in miners, and in stationary engineers who operate furnaces. Lead intoxication occurs from drinking water conveyed through lead pipes, from inhaling fumes containing lead in foundries, and where lead is being reclaimed by burning storage batteries. Arsenic exposure from fruit sprays, insecticides, and rodent poisons accidentally inhaled or ingested is a hazard. Arsenic is also an occupational hazard in some manufacturing processes making paints, dyes, chemicals, and glass. Mercury is occasionally a hazard in plants which manufacture mirrors, thermometers, barometers, and X-ray machines. But most frequently mercury intoxications occur in farmers who are exposed to fungicides (Ceresan) used for spraying seeds. Organic solvents such as trichlorethylene, carbon tetrachloride, and carbon disulfide are widely used in industry as degreasers, insecticide vehicles, cleaning agents, and chemical solvents; exposure to their vapors may produce severe symptoms. Accidental intoxications with these agents and intentional administration of poisons such as arsenic may cause a perplexing confusional state in this age range.

8. Endogenous intoxications produced by disease of the human body are a frequent cause of confusion. Uremia produces confusion associated with physical restlessness, muscle twitchings, and convulsions and is recognized by the uremic odor to the breath. Hepatic decompensation produces confusion which tends to be recurrent and is associated with spider nevi of the face and chest, ascites, edema of the limbs, and jaundice. The condition may be recognized by the "fetor hepaticus" which is a characteristic "fishy" odor to the breath. Carbon dioxide intoxication occurs in the presence of chronic respiratory disease such as emphysema and bronchiectasis. This condition can be recognized by the associated respiratory distress, the purplish plum color of polycythemia, and the tendency toward somnolence. Porphyria may produce recurrent episodes of confusion, especially in females between thirty and sixty years of age. This condition is associated with abdominal colic and peripheral neuritis and is recognized by the characteristic color of the urine.

Head injury. This is the next most common cause of a confusional state in this age group. The diagnosis has been discussed in the previous section. A complication of head injury, the subdural hematoma, is seen in the latter ages of this group. The clinical course is one of progressive confusion with the development of focal neurological deficit.

Examination may show only a mild mono- or hemiparesis with increased deep tendon reflexes. Signs of increased intracranial pressure, papilledema, slightly increased nuchal tone with dulling of sensorium, and a tendency to somnolence is the most common presenting symptom complex.

Laboratory examination by cerebral angiography is diagnostic; a skull X-ray showing a shift of a calcified pineal is useful if present. Treatment consists of surgical removal of the lesion.

CAUSES IN OLD AGE

Cerebrovascular disease. The most frequent cause of confusion in this age group is cerebrovascular disease, particularly cerebral infarction. Generally the confusion is of sudden onset and occurs during periods of inactivity. It is associated with focal neurological deficit of motor, sensory, visual, or speech function which, however, may be of a very subtle nature. The course is one of improvement, the deficit is greatest within hours after onset and then gradually clears.

Examination may reveal unilateral paresis associated with increased reflexes, loss of sensory appreciation from one side of the body, aphasia, or a visual field deficit of a homonymous type. Laboratory examination is of no help.

Treatment is directed toward detecting systemic diseases which are frequently etiologically significant in cerebral infarctions. An associated anemia is diagnosed and treated, cardiac arrhythmia or failure is detected and corrected, a relative hypotension is treated with elastic stockings and abdominal binders, and a partial occlusion of a major neck vessel may occasionally be found and warrants evaluation and surgical correction in selected cases.

Cerebral anoxia. The next most common cause of confusional state is cerebral anoxia aggravating preexisting vascular disease. Patients of this age group are prone to manifest confusion whenever cerebral oxygenation is reduced by such varied factors as pneumonias, hyperpyrexic states, prolonged supine position, hypotensive drugs, and anemia.

Examination in these cases reveals no focal neurological deficits but may show dyspnea, fever, low blood pressure, or pallor. Laboratory tests may confirm the presence of pneumonia or reduction of the oxygenation of the blood.

Toxins. Medications are a common cause of confusional state in the oldster. Tolerance for barbiturates, parkinsonian drugs, seizure medications, and anodynes is frequently greatly reduced. History of the initiation of any medication prior to the development of confusion should strongly implicate that agent as the cause of cerebral symptoms until proven otherwise.

Examination and laboratory tests are of no help. Treatment consists only of discontinuance of the medication and careful following of the patient to make certain that the course is one of gradual improvement. Recovery may be delayed for days or weeks in this age group, but the prognosis is generally good.

Head injury and subdural hematomas are a cause for the confusional state in this group. The diagnosis has been discussed in the previous section.

Senile deterioration. This poorly understood condition known as "senility" is also a cause of confusional state in this age range. The condition should be considered only if the more remedial causes have been excluded. This condition is one of slow onset and progressive course with no evidence of focal neurological deficit. Both a rapid onset and focal signs tend to make this diagnosis unlikely.

Examination in these cases should reveal no systemic disease or focal neurological abnormalities. Laboratory confirmation may be concluded if diffuse cerebral atrophy is seen by pneumoencephalography. Treatment consists of protecting the patient in a well supervised environment.

LAPAROTOMY FOR RECTAL CARCINOMA requires special precautions to prevent implantation of tumor cells. Recurrence from implantation and other causes emphasizes the value of examination at six months after operation and yearly thereafter for five years. Curative operations were performed on 800 patients from 1952 through 1955 with rectal carcinoma, but by mid-1961, 92 had local pelvic recurrence. When determined, the cause appeared to be implantation in 27 patients, direct extension in 10, involved nodes in 3, and lymph spread to other organs in 4.

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The Relation of Cancer to Allergy

KENNETH J. JOHNSON, M.D., M.S.
Bismarck

INTRODUCTION AND REVIEW OF THE LITERATURE

The concept that there might be some relationship between cancer and allergy was first implied when it was realized that cancer cells may be antigens. In studying the behavior of cancer these facts have been observed:

1. In a given histopathologic type of cancer, its clinical behavior will vary tremendously in various patients of the same age or sex or race (Koelsche[1]).

2. The clinical course of the cancer likewise sometimes is not correlated with the grade of malignancy (Koelsche[1]).

3. Some established tumors spontaneously regress (Koelsche[1]).

4. After incomplete removal of cancer, some patients survive long afterward (Koelsche[1]).

5. Sometimes, years after successful treatment of primary cancer, widespread metastatic growths appear (Koelsche,[1] Brown[2]).

6. Throughout life as many as one million body cells each day may undergo mutation (Burnet[3]).

7. Cancer cells have been shown to differ from other body cells immunologically (Black and Speer[4]).

8. Antibodies against cancer cells have been demonstrated (Graham and Graham[5]).

9. Properdin level is decreased in cancer patients (Rottine, Levy, and Conte[6]).

10. When the cancer is active the serum gamma globulin is increased (active immune mechanism), while in a cancer patient who is terminal the serum gamma globulin is decreased (breakdown of immune mechanism, Koelsche[7]).

11. Cancer cells injected into a fetal or neonatal animal are accepted by the animal with no subsequent formation of antibodies against it, whereas the same injection into an older (immunologically competent) animal of this species is rejected with formation of antibodies against it (Andervont[8]).

12. Tumor transplants undergo homograft rejection and second set reactions, just as does normal tissue (Koelsche[9]).

There is, then, definite evidence today to justify the thesis that cancer cells are or contain antigens. Southam[10] says the appearance of cancer represents a slip-up in the defense mechanism. Ratner[11] regards allergy as a battle against the invasion of foreign substances into the body. The clinical sensitiveness of an individual represents an intensive effort of the individual against the invading antigen (Spain[12]). Although the capacity to become sensitized or be allergic is held by all, Glaser[13] says, this sensitivity may vary in degree (Harkavy and Perlman[14]).

This mechanism of protection against cancer has been proposed by Thomas[15] to be that of the immunological one of delayed hypersensitivity. It has been shown that a patient may have his delayed hypersensitivity response altered but his immediate hypersensitivity response, with plasma cells, will remain intact—such as in sarcoid and Hodgkin's disease. On the other hand, a patient may have his immediate hypersensitivity response altered but his delayed hypersensitivity response, with lymphocytes, will remain intact—such as in hypogammaglobulinemia, as pointed out by Raffel.[16] A patient may have a delayed reactivity to an antigen at one time, followed later by immediate cutaneous reactivity; this transition occurs (at least with Ascaris antigen, as shown by Fisherman[17]) faster in atopic patients and slower in cancer patients than it does in nonatopic noncancerous patients. The incidence of atopic disease in patients who suffer from malignancy appears to be significantly below the incidence of atopic disease in noncancerous pa-

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KENNETH J. JOHNSON *is with the Quain and Ramstad Clinic, Bismarck*

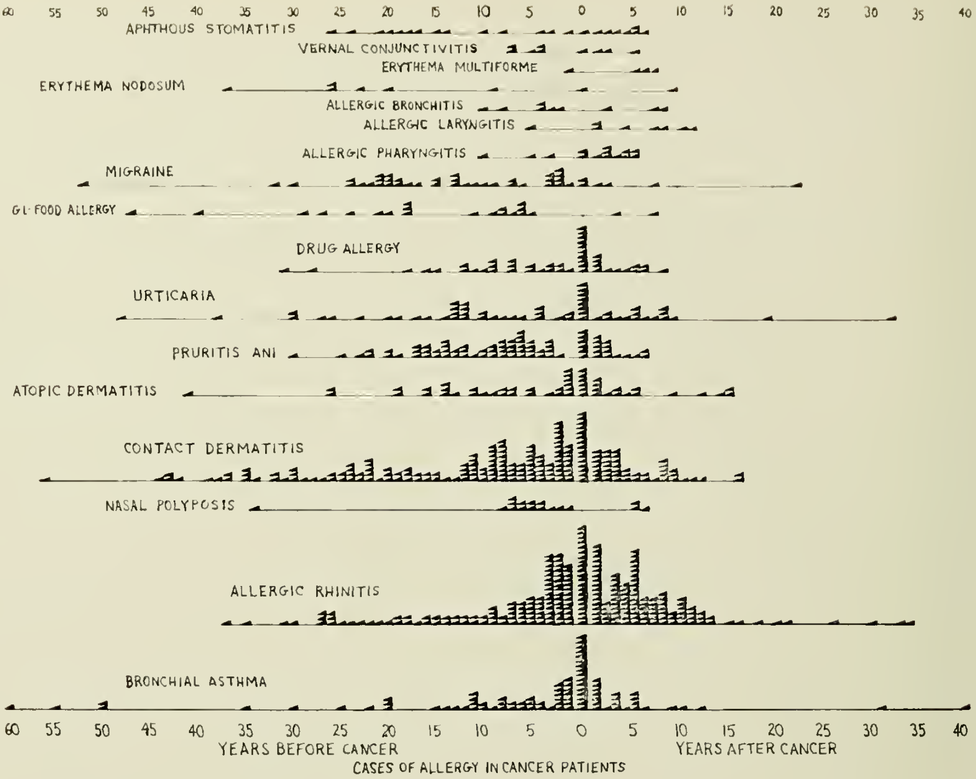

Fig. 1

tients, Fisherman[18] finds. What makes an individual atopic is his greater propensity for producing a peculiar antibody reagin; he also is especially good in transferring at least some sensitivities to normal skin, and he often produces antibodies more readily than normals do. These antibodies, however, are sometimes inferior (Raffel[19]).

ORIGINAL INVESTIGATION

To study the relation of cancer to allergy, the age of the patient when any allergy was diagnosed was noted in relation to the age when the malignancy was first diagnosed (and operated on if feasible) in 1,000 cancer patients seen in this clinic. These patients had been followed for as long as sixty-two years and had made as many as 790 visits to the clinic over that period of time. To eliminate any patients with whom contact had been lost, only those were considered who had been seen in the clinic sometime during 1960 to 1962. See figure 1.

Each dot represents a year in which that allergic manifestation was diagnosed one or more times in one patient; two dots in different years might refer to the same patient. For instance, if one patient visited the clinic several times in one year for the same allergy, such as allergic rhinitis, he was counted only once for that year for that allergy. If he visited the clinic the next year for that same allergy, he was counted only once for that next year for his allergic rhinitis. If during that year he also was seen for asthma, he was counted once for his asthma and once for his allergic rhinitis for that year. Thus, there was a total of 906 allergy manifestations recognized in those years, in a total of 379 of the 1,000 cancer patients studied. Allergic manifestations, or those which repeatedly have been claimed to be allergic in nature, which were too infrequent to be included in figure 1 were: physical allergy to cold, 1 case same year as cancer diagnosis; physical allergy to sun, 1 case one year after and 1 case five years after; allergic reaction to insect sting, 1 case six years after; blood transfusion reaction, 1 case in year of cancer diagnosis; periarteritis nodosa, 1 questionable case in year of cancer diagnosis; ulcerative colitis, 1 case eleven years before and another case two years and twenty-nine years before cancer; Hashimoto's struma, 1 four years before cancer; Henoch's purpura, 1 case two and one years before and the same year of the cancer; multiple sclerosis, 1 case eight years before cancer; lupus erythematosus, 1 case thirty years before, 2 cases seven years before, 1 case three years after, and 1 case six years after cancer.

In classification, hay fever and nonseasonal allergic rhinitis were grouped together, since in some cases it was uncertain from the doctor's notes whether the allergic rhinitis was seasonal. Contact dermatitis included dermatitis venenata, poison ivy, and adult eczema; atopic dermatitis included childhood eczema, neurodermatitis, and dermatitis due to inhaled pollen. If the type of allergic dermatitis was uncertain from the physician's notes it was classified as contact dermatitis if the patient was over 20 years of age at that time or atopic dermatitis if he was under age 20. Urticaria included angioneurotic edema and 3 cases of dermographia. Drug allergy included dermatitis medicamentosa and other drug reactions definitely allergic in nature. Gastrointestinal food allergy was diagnosed when the notes stated the patient got indigestion from peanuts, lettuce, chocolate, nuts, wheat, milk, fish—those foods to which intolerance is infrequent enough to be considered an allergy, but was not diagnosed if indigestion resulted from pork, cream, fats, spices, or sausage, which typify gallbladder disease or peptic ulcer.

When we consider when these allergic manifestations occurred in relation to when the cancer was diagnosed we find that in every diagnosis except migraine, erythema nodosum, and gastrointestinal food allergy the great majority of them occurred within ten years before or after the cancer diagnosis. See table 1. Also note in figure 1 that more allergy was diagnosed during the year cancer was diagnosed than in any other year.

This is in contrast to the findings of Fisherman,[18] who found that in atopic patients with cancer the atopic symptoms usually lessened or disappeared at least ten years before the recognition of malignancy. He also found the incidence of atopy (bronchial asthma, allergic rhinitis, and atopic flexural eczema) in patients with malignant tumors to be 3.2%; in my series the incidence is 18.5%. What accounts for these discrepancies? My cases of bronchial asthma include those of infectious etiology, and his did not; he included only seasonal allergic rhinitis, while I include both seasonal and nonseasonal allergic rhinitis; my diagnoses of atopic dermatitis probably are more inclusive than his. Moreover, his series was derived from histories obtained from interviewing patients attending medical school clinics; my series was derived from notes made by physicians who had seen and examined the patients on numerous occasions over many years. It is reasonable that many patients forget, or never learned, that they had had allergic manifestations. Care was taken in studying this clinic's physicians' notes not to be prejudiced in diagnosing allergy. None of those physicians were particularly interested or trained in allergy.

TABLE 1

NUMBER AND TIME OF ALLERGY DIAGNOSES, TAKEN FROM FIG. 1

Allergy diagnosis	*Over 10 years before or after cancer diagnosis*	*Ten or less years before or after cancer diagnosis*
Bronchial asthma	23	65
Allergic rhinitis	53	180
Nasal polypi	0	16
Contact dermatitis	68	120
Atopic dermatitis	17	34
Pruritus ani	25	50
Urticaria	22	34
Drug allergy	8	37
Gastrointestinal-food allergy	11	10
Migraine	25	18
Erythema nodosum	5	3
Erythema multiforme	0	4
Allergic bronchitis	0	9
Allergic laryngitis	1	8
Allergic pharyngitis	0	14
Allergic conjunctivitis	0	9
Henoch's purpura	0	4
Lupus erythematosus	1	4
Aphthous stomatitis	9	13
Miscellaneous (see text)	0	6
TOTAL	268	638

Nevertheless, it was felt essential that a series of 1,000 patients be selected without bias for any factor except that they never had cancer, to serve as a basis for comparison. This control series was selected by drawing from the record files consecutively, without regard to other diagnoses, a matching number of noncancerous patients' records for each letter of the alphabet with which the cancer patients' last names started. If an inequity resulted in the number of clinic visits or the number of years the patients were seen in the clinic, records of other noncancer patients were then drawn from the files consecutively without regard to other diagnoses, until the 2 series matched each other for number first appearing at the clinic in each ten-year period and for total number of clinic visits. Entrance to a hospital was considered as 1 visit, and discharge from the hospital as the next 1 visit; prenatal visits and delivery were all counted as 1 visit; a fracture record was counted as 1 visit; eye department visits were counted once, and then only if an allergy was diagnosed there; a newborn until he was discharged from the hospital was considered as 1 visit. All patients selected were seen in the clinic sometime between 1960 and 1963. This method resulted in 2 series of patients as compared in table 2 and table 3.

Statistical analysis showed the data of table

TABLE 2

VALIDITY OF NONCANCEROUS PATIENTS AS CONTROLS

(Distribution of Cancer and Noncancer Patients by Total Number of Clinic Visits)

Total number clinic visits	*Cancer series*	*Control series*	*Total number clinic visits*	*Cancer series*	*Control series*
1- 10	254	251	191-200	3	1
11- 20	202	202	201-210	2	3
21- 30	134	134	211-220	2	1
31- 40	111	114	221-230	1	1
41- 50	69	82	231-240	1	1
51- 60	39	46	241-250	2	2
61- 70	43	34	251-260	0	3
71- 80	29	28	261-270	1	1
81- 90	21	23	271-280	0	1
91-100	14	18	281-290	1	1
101-110	12	10	291-300	0	0
111-120	14	7	301-350	2	1
121-130	9	7	351-400	2	1
131-140	9	7	401-450	2	2
141-150	7	5	451-500	1	1
151-160	2	4	501-550	1	0
161-170	2	4	551-600	0	0
171-180	4	2	601-700	0	1
181-190	3	1	701-800	1	0
TOTAL				1,000	1,000

TABLE 3

VALIDITY OF NONCANCEROUS PATIENTS AS CONTROLS

(Distribution of Cancer and Noncancer Patients by Year of First Clinic Visit)

Year of first clinic visit	*Cancer series*	*Control series*
1900-1907	3	2
1908-1912	22	19
1913-1917	50	31
1918-1922	43	46
1923-1927	81	84
1928-1932	67	84
1933-1937	77	88
1938-1942	78	107
1943-1947	133	126
1948-1952	123	115
1953-1957	135	121
1958-1962	188	177
TOTAL	1,000	1,000

2 to have $P > 0.95$ and of table 3 $P > 0.20$; from this I conclude that the 2 series are comparable as to number of clinic visits and number of years followed in the clinic, so that if one group shows a greater number of allergies it will not be due to the patients having been seen more often than those of the other group. When these 1,000 noncancerous control patients were analyzed (see Table 4) allergy was found in 478 patients; it was even more common in the controls than in the cancer patients (in agreement with Fisherman's findings[18]), in ratios of from 1+ to 1 (such as in nasal polypi, 11 control patients and 9 cancer patients) to 3 to 1 (such as in allergic bronchitis, 17 control patients and 6 cancer patients). The frequency of allergy in the control series is significantly greater than the frequency of allergy in the cancer series: by statistical analysis $t = 22.13$ and $P < 0.001$.

Incidentally, the mortality was 122 for the cancer patients and 17 for the controls; 12 of the former and 11 of the latter had tuberculosis, which would imply that cancer and tuberculosis do not influence each other.

The patients in both groups were often seen repeatedly for the same diagnosis, of course; counting as one the number of clinic visits made for each allergy diagnosis in one calendar year, as explained above for the cancer patients, the total number of visits made for all allergies was 906 in the cancer patients and 1,259 in the noncancerous patients. See table 5.

The types of cancer the 1,000 cancer patients had are shown in table 6. Note that there is no significant difference in the proportion of patients in each group who received allergy diagnoses: $P = 0.30$. See table 6.

The total number of cancer patients in table 6 is greater than 1,000 and total number of those patients with allergy is higher than the figure (379) given in table 5 because some of the patients had more than 1 cancer, and some had more than 1 allergy. One hundred thirty-five cancer patients each had from 2 to 9 distinct malignancies. One hundred and forty-one cancer patients each had from 2 to 6 distinct allergies. Three of these had 6 distinct allergies. One patient had drug allergy, bronchial asthma, neurodermatitis, allergic bronchitis, contact dermatitis, and migraine in a space of ten years, during which time she had a squamous-cell carcinoma of the skin. Another patient had drug allergy, neurodermatitis, allergic rhinitis, migraine, food allergy, and contact dermatitis in a space of twenty-nine years, all before she developed adenocarcinoma of the uterus. The third patient had urticaria, allergic bronchitis, allergic rhinitis, contact dermatitis, aphthous stomatitis, and vernal conjunctivitis over a space of twenty-seven years, all before she developed a basal-cell carcinoma of the skin.

DISCUSSION AND SPECULATION

Previous reports have given the incidence of allergy in the general population as around 10% (Peshkin[20]) to 20% (Siegel and Seideman[21]), or 22.8% in a pediatric population (Szanton, Rapaport, and Appel[22]), or 50% if subclinical or minor allergies are included (Vaughn,[23] Ratner and Silberman[24]). In my series 47.8% of the non-

TABLE 4

FREQUENCY OF ALLERGY

(Distribution of Cancer and Noncancer Patients by Type of Allergy They Had)

Number of patients with	*Cancer series*	*Control series*
Bronchial asthma	41	58
Allergic rhinitis	135	194
Nasal polypi	9	11
Contact dermatitis	116	142
Atopic dermatitis	36	55
Pruritus ani	41	68
Drug allergy	45	70
Gastrointestinal-food allergy	21	28
Migraine	35	39
Allergic conjunctivitis	6	14
Aphthous stomatitis	12	22
Allergic pharyngitis	13	15
Allergic laryngitis	6	9
Allergic bronchitis	6	17
Urticaria	36	53
Physical allergy to cold	1	0
Physical allergy to sun	2	1
Allergic reaction to insect sting	1	0
Blood transfusion reaction	1	2
Periarteritis nodosa	1(?)	0
Lupus erythematosus	6	1
Geographic tongue	0	1
Erythema multiforme	4	3
Temporal arteritis	0	1
Erythema nodosum	3	2
Allergic purpura	1	2
Ulcerative colitis	2	6
Cystic fibrosis	0	1
Hashimoto's struma	1	0
TOTAL	581	815
AVERAGE	20.03	28.10

TABLE 5

COMPARISON OF INCIDENCE OF ALLERGIES

Number of	*Cancer series*	*Control series*
Patients with allergies	379	478
Allergies they had	581	815
Years in which they made clinic visits for these allergies	906	1,259

cancerous patients had clinical allergies, in the sense that a complaint was made by the patient, and an allergy diagnosis was made by the attending physician or by me after reading his notes.

There is no sharp dividing line between allergic and nonallergic individuals. Allergic reaction is a matter of threshold; Prickman[25] claims that all people may be sensitized under certain circumstances, and Ratner and Silberman[24] state that all individuals are potentially capable of developing an allergy. It is logical that the longer and more closely a given person is observed the more likely it will be that an allergic manifestation will be noted, therefore. I would surmise that if all people could be examined at all times throughout their lives, most of them would show at least one of the thirty-odd above listed (Table 4) allergic manifestations at some time or other.

From studying figure 1 it would seem that something happens to the immune mechanism during the period of life that the patient develops cancer, which increases his responsiveness to foreign material, as evidenced by increased activity of immediate type hypersensitivity (cf. Lamb, Pilney, Kelly, and Good[26]), in contrast to his previous activity which had been less than that of the noncancerous population. However, it would seem, while this increased activity of the immediate type hypersensitivity mechanism is occurring, the delayed type hypersensitivity becomes underactive, inasmuch as cancer cells are allowed to grow instead of being destroyed as they previously were being destroyed (Crowle[27]).

If the delayed type of hypersensitivity becomes "sluggish" it allows abnormal cells to proliferate (Green[28]) and we find cancer growing. If it becomes "overexuberant" it attacks body cells which we feel are innocent, and we diagnose an autoimmune disease such as lupus erythematosus (Harvey[29]), or it gives skin reactions where articles of adornment or products of commerce, substances we consider harmless and beneficial, contact our skin. And as we grow older, live longer, and take longer to wear out, and as our civilization places us in more and more contact with the chemicals we manufacture (cf. Randolph[30]), it will become more likely that our delayed type of hypersensitivity mechanism will seem to be malfunctioning at some time or other.

Allergy and cancer are two maladies of adaptation, Kousmine and Strojewski-Guex[31] say, different in their clinical manifestations but very similar in nature. Since the plasma cell, which produces antibody and mediates immediate type hypersensitivity, is derived from the lymphocyte (Wintrobe[32]), which mediates delayed type hypersensitivity, it is plausible that delayed type hypersensitivity may be a more primitive im-

TABLE 6

FREQUENCY OF ALLERGY WITH EACH TYPE OF CANCER

Type of cancer	*Number of cancer patients*	*Number of these patients with allergy*	*Percentage of these with allergy*
Lungs	27	12	44%
Gynecological	115	41	36%
Breast	152	67	44%
Genitourinary	125	40	33%
Gastrointestinal	162	47	29%
Skin	455	147	32%
Miscellaneous	137	46	34%
TOTALS	1,173	400	34%

munological mechanism and also that delayed type hypersensitivity appears first (Ratner, Crawford, Feldman, and Krimli[33]) and could be considered a first line of defense. The second line of defense, then, would be immediate type hypersensitivity. If any cancer cells elude the first line of defense the second line of defense might be manifested by appearance of anticancer antibodies, the product of plasma cells. Evidence for these was cited at the beginning of this article.

Berdel[34] theorizes a more complicated arrangement. An atoxic antigen, which in our present consideration is a cancer mutation, invokes formation of an antibody which is toxin-forming. The two combine to produce a toxic antigen-antibody reaction, which causes the host to become sensitized against the original antigen, the cancer, which is destroyed. However, the toxin formed stimulates production of another antibody, the antitoxic antibody, which combines with the toxin-forming antibody to produce an atoxic antigen-antibody-antitoxin reaction. This second reaction desensitizes the host against the original antigen. If a second similar mutation occurs soon after the first, and before the antitoxic antibodies disappear, these combine with the toxin-forming antibodies and prevent them from combining with and destroying the cancer cells, so the cancer grows.

In conclusion, it is proposed, hypothetically, that cancer is due to underactivity and allergy to over-activity of the immunologic mechanism. The following diagram is proposed, hypothetically to illustrate the relation of cancer to allergy:

	Immediate hypersensitivity	Delayed hypersensitivity
Overactive:	atopy	contact dermatitis
Underactive:	hypogamma-globulinemia	cancer, sarcoidosis, Hodgkin's disease

SUMMARY

1. The incidence of allergy in 1,000 cancer patients is compared to that in 1,000 noncancerous patients. The 2 groups were matched as to number of years seen in the clinic, with a maximum of sixty-two years, and as to number of clinic visits made, with a maximum of 790 visits.

2. A total of 37.9% of cancer patients and 47.8% of noncancerous patients had one or more allergies at some time.

3. Most of the allergy occurring in the cancer patients was manifested between ten years before and ten years after the time of diagnosis of the cancer.

4. More allergy was found in the year that cancer was diagnosed than was found in any other year.

5. The cancer patients had significantly less allergy than noncancerous patients.

6. One type of cancer is not associated with allergy more than any other type, according to this data.

7. Cancer cells are or contain antigens, against which, it is surmised, first the delayed type and then the immediate type of hypersensitivity may be utilized by the host as defense.

8. It is proposed (purely hypothetical) that cancer is due to underactivity and allergy to overactivity of the immunologic mechanism.

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PARTIAL OR TOTAL aortic valve replacement with Teflon cusps often leads to aortic insufficiency due to prosthetic failure. The results of replacement procedures in 36 patients with acquired aortic valve disease in 1962 were evaluated; 5 late deaths had occurred. An additional 5 late deaths occurred among 12 patients having Teflon cusps inserted before 1962. Eight postmortem examinations showed changes such as infection or partial dehiscence of suture lines, fracture or decreased cusp mobility, thrombosis of the ascending aorta, and multiple peripheral emboli. Valvular function was competent in 20 of 23 patients at dismissal but in only 11 at follow-up.

RICHARD E. LARSON, M.D., and JOHN W. KIRKLIN, M.D., Mayo Clinic and Foundation, Rochester, Minn. Early and late results of total and partial replacement of the aortic valve with individual Teflon cusps. J. thorac. cardiovasc. Surg. 47:720-724, 1964.

ROUTINE THYROTROPHIN TESTING of all patients with spontaneous myxedema probably would reveal a higher than suspected incidence of isolated thyrotrophin deficiency. The test differentiates from primary hypothyroidism; history, physical, and laboratory data do not. Technique involves measurement of I^{131} twenty-four-hour uptake before and after 5 to 10 I.U. of intramuscular thyroid-stimulating hormone (Thytropar®). Rise in protein-bound iodine after Thytropar® also is useful in diagnosis. The diagnostic techniques have been used in 3 patients with isolated thyrotrophin deficiency who presented with clinical and laboratory findings of myxedema. Thyroid replacement therapy was successfully used for three to six years.

FRANCIS N. LOHRENZ, M.D., RAFAEL FERNANDEZ, M.D., and RICHARD P. DOE, M.D., Veterans Hospital and University of Minnesota, Minneapolis. Isolated thyrotrophin deficiency. Ann. intern. Med. 60:990-998, 1964.

Rheumatic Heart Disease

Newer Concepts in Diagnosis, Treatment, and Prevention

ROBERT S. ELIOT, M.D.

Minneapolis

RHEUMATIC FEVER is very similar to a candle and its drippings (Fig. 1). The lighted candle symbolizes acute rheumatic activity. The wax drippings indicate old or developing endocarditic changes and thickening of the heart valves and chordae. The candle may burn for a time and become extinguished for many years. Later, the candle may again be lighted and the waxy drippings may again be deposited at the base of the candle, indicating increasing extent and severity of pathologic changes in the valves and chordae. It is the problem of the physician to recognize when the candle is lit, to seek the proper means of extinguishing the flame, and, having done so, to prevent the flame from being ignited again.

It is the purpose of this article to indicate some of the advances and some of the problems in the recognition, treatment, and prevention of rheumatic fever, with special reference to the management by the family physician.

DIAGNOSIS

First of all, we recognize rheumatic fever in the same manner that we have in the past twenty years. Minor modifications have been made in the Jones criteria by the use of newly devised laboratory tests. These laboratory tests, however, usually tell us only if the streptococcal infection has been present. They do not indicate the presence of rheumatic activity specifically.

One newer laboratory test for the sole purpose of detecting the presence of streptococcal infection is the antideoxyribonucleic acid "ase" B (anti-DNAase-B) determination. This is a newly recognized antibody which is not only found early in rheumatic activity but also has a tendency to remain for a period of months following an active streptococcal infection. The addition of this new antibody test to our diagnostic armamentarium has in the opinion of Wannamaker,[1] among others, given us a new major criterion to be included among those in the usual Jones criteria for rheumatic activity.

The means of determining recent streptococcal infection have improved. Naturally, the antistreptolysin O (ASO) titer is still of great value and continues to be of primary importance. The higher apparent reliability of the anti-DNAase-B test compared to ASO titers, however, indicates that the former may become more popular.

CLINICAL EVALUATION

As we consider the problem of clinical evaluation of the patient thought to have rheumatic carditis, there are certain features of the illness which recently have been found to be of value in determining treatment and prognosis. In general, it has been thought that rheumatic fever affects a given individual in the same way for the acute and each recurrent attack. His response to the rheumatic strains of streptococci is thought to be as specific and reproducible as his fingerprint; that is, if an individual who is experiencing an acute episode of rheumatic fever has involvement primarily of the joints, without any evidence of myocarditis, the chances are excellent that recurrent episodes will be of a similar nature. There are other individuals who experience carditis but with mild or no evidence of arthritis. The latter individuals require much closer clinical observation, since they are much more apt to have recurrent episodes of carditis resulting in rheumatic valvular deformity.

Because of this phenomenon, some clinicians have recommended that the patient who has evidence of only polyarthritis receive penicillin only for acute respiratory illnesses. On the other

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ROBERT S. ELIOT *is a cardiologist from the Department of Medicine, University of Minnesota, Minneapolis.*

Guest lecturer for North Dakota Heart Association in 1964 and 1965. Presented in Grand Forks, Devils Lake, Minot, and Williston on Feb. 3-7, 1964, in Jamestown, Bismarck, and Dickinson on Feb. 1-3, 1965, and in Fargo on Feb. 22, 1965.

Fig. 1. A lighted candle symbolizing acute rheumatic activity. The wax drippings indicate old or developing endocarditic changes. The flame indicates rheumatic activity. Photograph courtesy of Dr. Jesse E. Edwards

hand, they recommend that the individual in whom carditis occurs should receive prophylactic penicillin to prevent acute respiratory infections. I would like to advance my opinion.

It is apparent that patients who present with rheumatic valvular disease do not universally give a history of acute rheumatic fever. Only about half of such patients give historical evidence of an acute episode of rheumatic fever. We must assume that some members of a group of patients who are thought to have rheumatic fever but with only polyarthritis and without carditis may, in fact, also have experienced a clinically undetected cardiac inflammatory activity. I feel, therefore, that no differentiation should be made regarding institution of a rheumatic fever prophylactic program between those rheumatic patients manifesting carditis and those who appear to have only arthritis.

TREATMENT OF ACUTE PHASE

In the patient with acute rheumatic fever, what then is the treatment of choice? This is currently being debated. Should only steroids be used? Should aspirin alone or in conjunction with steroids be used? It might be said that the advantages and disadvantages of one medical treatment over another follow the following rule: "The duration and heat of the debate is inversely proportional to the value of one treatment over the other." At the present time, many complications result from steroid treatment. As yet, benefits are difficult to prove. In the treatment of active carditis, most of us would agree on the use of aspirin and steroids. The superiority of combined treatments for acute rheumatic fever, however, is very difficult to prove.

PROPHYLACTIC TREATMENT

The preferred prophylactic agent against recurrence of active rheumatic fever at the present, as recommended by the American Heart Association's Council on Rheumatic Fever and Congenital Heart Disease, is intramuscular administration of benzathine penicillin G once every thirty days for an indefinite period of time.[2] In patients who object to intramuscular therapy, 250,000 units of penicillin G may be given orally twice daily, indefinitely. For those allergic to penicillin, sulfadiazine given orally in doses of 0.5 gm. twice daily is recommended, indefinitely.

These medications are made available to patients in North Dakota at reduced cost through the cooperative efforts of the Heart Disease Control Program of the North Dakota Public Health Service and the North Dakota Heart Association.

INCIDENCE

Most clinicians and investigators have the impression that they are seeing or hearing of fewer instances of acute rheumatic fever than in years gone by. In North Dakota, however, 200 new cases are reported each year. It is probable that an equal number are subclinical or go undetected. It has been estimated that each such case represents an expense of $20,000. This figure is based upon the cost of medical attention, disability, hospitalization, insurance, and lost wages.

CHRONIC RHEUMATIC VALVULAR DISEASE

Some of the clinical features of various forms of rheumatic heart disease have been most helpful in diagnosis, as have new diagnostic techniques.

Mitral valve. Most common of all is involvement of the mitral valve. How much mitral valve disease does it take before an operation should be done? What operation is best suited for the particular condition in a given patient? Two clinical signs have been said to be of great importance in determining the state of pliability of the mitral valve.

First, the intensity of the first mitral heart sound is said to be a good indication of a pliable mitral valve. Second, an opening snap is also considered to represent pliability.

The loud M_1 is frequently ascribed to the thickened anterior and posterior leaflets of the mitral valve slapping together during the early phase of ventricular contraction; the opening snap, on the other hand, is usually ascribed to the sudden opening of the rigid mitral valve.

From the pathologic standpoint, there is much to invalidate these explanations. A loud M_1 can be present in a valve which is so heavily thickened and calcified that movement of the valve, including its fused cusps, is a mechanical impossibility. Under these circumstances, the loud first mitral heart sound is possibly the result of stretching the chordae tendineae during early left ventricular systole rather than leaflet contact.

By the same reasoning, if such a valve cannot open, how then can there be an opening snap? The opening snap may, in fact, be due to the sail-like whipping of the anterior leaflet of the mitral valve. It is not possible, then, to accurately determine pliability of the mitral valve from the opening snap or the loud M_1.

As can be noted from pathologic specimens, there is a definite thickening and shortening of the chordae in the mitral valve which is involved with chronic rheumatic changes (Fig. 2). There is, then, a propensity of the chordae to hold the two leaflets of the mitral valve in a template-like fashion. Thus, even if it were possible to temporarily separate the two leaflets of the mitral valve by commissurotomy, they should approximate and fuse almost immediately. Further, when the surgeon approaches such a mitral valve from the left atrium by closed mitral commissurotomy, he cannot see the pathologic changes below the valve which are, of course, most important to success or failure of mitral commissurotomy.

The mitral valve, then, shows the surgeon its best face. It does so by hiding from him the appearance of the chordae tendineae, the appearance of the papillary muscles, and the distortion of the left ventricular surface of the mitral valve. It is these factors which primarily prevent the mitral valve from opening or cause it to stay in a fixed position once commissurotomy has been accomplished (Fig. 3). It is these factors that have made us reexamine our experiences with closed mitral commissurotomy.

Naturally, many would not be alive today were it not for the success of closed mitral commissurotomy, but it should be considered a palliative procedure. Aside from unrelieved stenosis, mitral incompetence has often resulted. This complication may occur when a mitral valve under tension from shortened chordae below the valve is opened. Further, the capable surgeon occasionally may separate parts of the valve which are not anatomically related to the commissure itself. Such false commissurotomies resulting in false orifices have also been a cause of mitral incompetence, substituting for or adding to the original mitral stenosis.

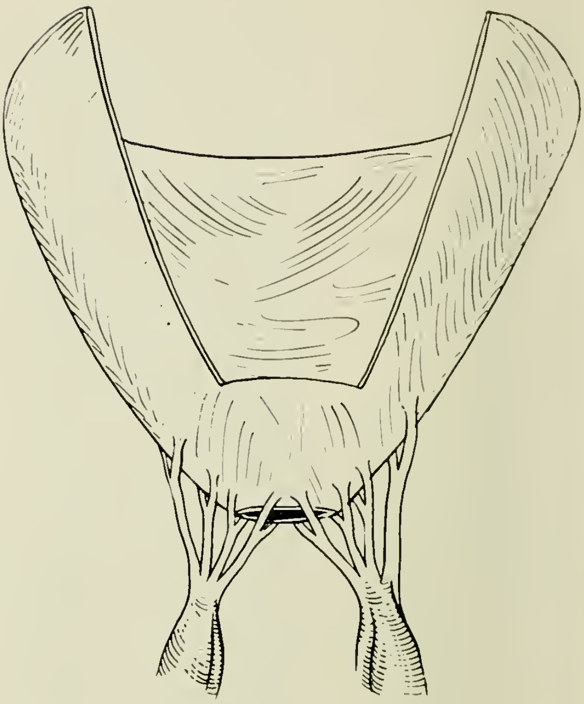

Fig. 2. Diagram showing the funnel-shaped left atrium with a stenotic mitral orifice. Below the valve are thickened and shortened chordae attached to papillary muscles. It is apparent that the shortening and thickening of the chordae cannot be visualized at the time of open or closed commissurotomy when approached from the left atrium.

Physiologic studies on patients before and after mitral commissurotomy have indicated something which is, at the present time, unexplained. That is, the cardiac output tends to remain fixed in most patients following mitral commissurotomy. It is the rare postoperative patient who has freedom from this fixation of cardiac output. The output may occasionally be fixed at a higher level, but rarely does it approach normal. It may be considered that this phenomenon is a result of the changes in the pulmonary vascular bed which prevent the adequate flow of blood to the left heart. There is evidence, however, to show that the majority of patients with mitral stenosis do not have a severe enough degree of pulmonary arteriolar changes to validate this theory. In general, the patient with rheumatic mitral stenosis has potentially reversible pulmonary arteriolar changes.

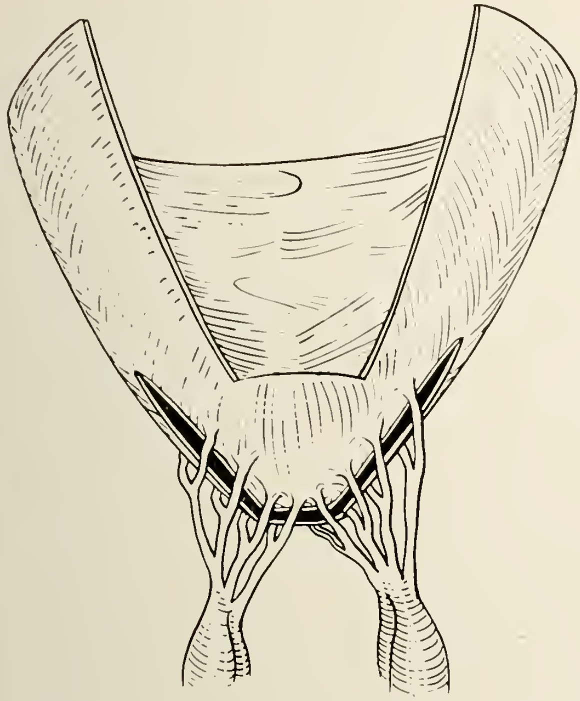

Fig. 3. Diagrammatic representation of the left atrium, chordae, and papillary muscles following bilateral mitral commissurotomy. The anterior leaflet of the mitral valve is cut away. The chordae tendineae, which are shortened and thickened, are not visible from the left atrial funnel-shaped surface. The chordae tend to hold the separated anterior and posterior leaflets of the mitral valve in such a fashion that adequate separation cannot be maintained because of the rigidity of these structures. Because of the rigidity of these structures, the anterior and posterior leaflets of the mitral valve are held in template-like fashion, which frequently brings about restenosis within a very brief period of time.

It is probable that there is some change which occurs at a distance from the heart which has to do with the ability of the body to use oxygen. Oxygen exchange in such patients having mitral stenosis is similar to that in highly trained athletes; both can drop their venous oxygen tensions from normal levels to as low as 35 to 40% saturation. In summary, then, suitable mitral commissurotomy at surgery is infrequently followed by significant physiologic improvement. It appears to be a temporizing, palliative procedure.

Mitral incompetence. In the patient with mitral incompetence, it is difficult to assess clinically the relative amounts of mitral stenosis and regurgitation. The most valuable signs for determining significant mitral incompetence are worth reviewing. First, the softness of the first mitral heart sound is helpful, but the sound can often be loud in patients having significant mitral incompetence. Next, the presence of a holosystolic murmur which radiates well into the midaxillary line is of great value, especially if there is no change with respiration. One of the most valuable signs of significant mitral regurgitation, however, is the presence of a third heart sound. The third sound is best heard at the apex. It has been our observation that angiographic studies tend to confirm the validity of this particular sign. It is considered to be an important one because it is one of the best indications that a patient is not a candidate for closed mitral commissurotomy. The third heart sound is generally considered to be generated by sudden distension of the left ventricle at the time of rapid filling. Whatever the mechanism, it should be remembered that this is an extremely valuable sign indicating significant mitral incompetence.

Another sign which tends to differentiate between predominant mitral stenosis and regurgitation is the precordial activity. In mitral stenosis, precordial activity tends to be quiet. Even less activity might be expected than occurs in the normal. In significant mitral regurgitation, however, there is usually a prominent and active down-and-out thrust of the left ventricle. It is thus frequently possible to differentiate between predominant mitral stenosis and regurgitation on the basis of activity of the precordial pulsations.

The treatment of a patient with significant mitral incompetence involves extensive surgery. Closed procedures are not indicated. Results with Ivalon spindles, with reconstruction of the valve by plastic measures, and with other surgical techniques have been relatively unsuccessful. Ball-valve replacement in mitral incompetence appears to be the surgical treatment of choice. Currently, our cardiac surgeons are employing the Starr-Edwards prosthesis in the mitral valve (Figs. 4 and 5). The incidence of death following this procedure has been progressively diminished. The risk of operation has decreased to a point where it may now be considered in patients who are at a stage where they fail to respond to medical treatment for mitral incompetence. This valve is employed in patients with mitral regurgitation or with calcific mitral stenosis who are functional class III or even IV. Significant reduction in the size of the left atrium has been noted within a period of one year from the time of operation in patients who have had predominant mitral incompetence repaired by ball-valve prosthesis. Postoperatively, some residual pressure gradient usually exists across the valve, partly as a result of inertia of the ball and partly because of the size of the orifice.

Aortic stenosis. In the patient with aortic stenosis as a result of rheumatic heart disease,

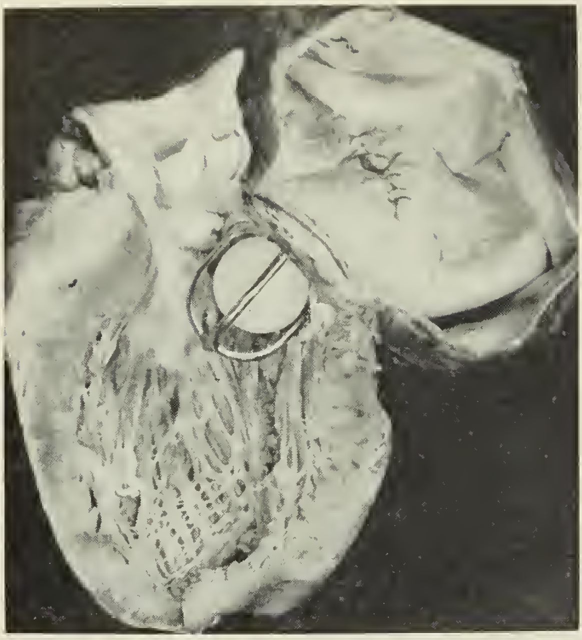

Fig. 4. Sagittal section through the left side of the heart showing the left atrium, a Starr-Edwards prosthesis in the mitral annulus, the left ventricle, the outflow tract of the left ventricle, the aortic valve, and the first portion of the ascending aorta. The Starr-Edwards prosthesis is sutured into position in the mitral annulus between the left atrium and the left ventricle. During diastole, the ball moves toward the apex of the birdcage allowing blood to flow from the left atrium to the left ventricle. During ventricular systole, the ball seats against the base of the birdcage, preventing reflux into the left atrium.

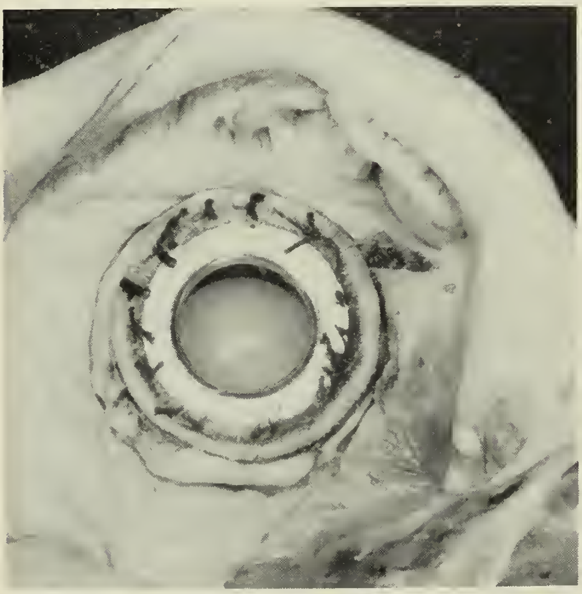

Fig. 5. The open left atrium showing the left atrial surface of a Starr-Edwards prosthesis placed in the mitral area, sutured into position. The ball can be seen to be at the apex of the birdcage in a position it would take during diastole.

a number of interesting features have recently been observed and must be considered by the clinician. First, many patients thought to have rheumatic aortic stenosis actually have a congenital valvular deformity. In the patient who presents with the classic finding of aortic stenosis, then, it is important to determine whether mitral valve disease is present also. If mitral valve disease is present, the probability of a rheumatic diagnosis is high. If there is no rheumatic valvular disease demonstrable, one must strongly consider that the lesion is on a congenital basis. This, of course, is especially true in female patients since [1] the incidence of pure rheumatic aortic valve disease in females is extremely low and [2] they almost always have associated mitral valve disease.

Rheumatic activity is not a consideration in congenital aortic stenosis. Therefore, prophylaxis is not necessary since it may [1] mask bacterial endocarditis and [2] cause a patient to become allergic to a drug which may be needed later.

Clinically, there are certain findings which are of value in assessing the significance of aortic valve stenosis. Basically, aortic stenosis and aortic incompetence present as two entirely separate clinical pictures. The patient with aortic stenosis generally has periods of dyspnea on exertion which are relieved by rest and strongly suggest the type of history obtained in mitral stenosis. Often accompanying the long history of dyspnea, however, is the associated complaint of chest pain. When chest pain occurs, it is due to a number of causes. First, there may be associated coronary artery disease, but angina pectoris may occur as a part of the syndrome of aortic stenosis itself. Also, there may be calcific extensions from the aortic valve which extend up the ascending aorta to involve coronary ostia. Further, these calcific nodules may occasionally become dislodged from the aortic valve and be thrown off as emboli to the coronary arteries. Naturally, the same route may be taken by bacterial vegetations originating on the aortic valve.

A familiar and extremely important sign in the patient with aortic stenosis is syncope. When syncope develops, it must be considered a grave prognostic indication requiring immediate consideration; 25% of patients with aortic stenosis die unexpectedly and suddenly after having one or more syncopal episodes. At least 12 of our patients with aortic stenosis have died unexpectedly while hospitalized awaiting ball-valve replacement surgery. The cause of death is believed to be a ventricular arrhythmia secondary to poor coronary arterial perfusion. This has been confirmed in 3 cases. Such a patient having signs of severe aortic stenosis should be considered in the same class as a patient with a malignant disease, for certainly, if operation is not performed, the risk of death is quite high. The treatment of choice is surgical replacement of the aortic valve.

Of critical importance to the clinician in determining the significance of aortic stenosis is the physical sign of an ejection click. It is true that if the cardiac output is normal the presence or absence of an ejection click is an important hemodynamic sign. If the ejection click is present, it usually indicates a gradient of less than 80 mm. Hg between the left ventricle and the ascending aorta. The later the ejection click, the more severe the stenosis. If, on the other hand, there is no ejection click, the degree of aortic stenosis is probably quite significant and severe. In the latter, the gradient is usually more than 80 mm. Hg between the left ventricle and the aorta.

Naturally, the shape of the murmur of aortic stenosis is also of importance. We recognize it to be diamond-shaped on the phonocardiogram. The later the peak of the diamond, the more severe the stenosis, and vice versa. These are signs which do not require instrumentation; they are, in general, available at bedside and aid in determining appropriate diagnosis. They are less accurate, however, if cardiac output is reduced.

Aortic regurgitation. The patient with aortic regurgitation has an entirely different clinical picture than the one with aortic stenosis. Such patients can be unaware of heart disease until left-sided failure develops. Until failure intervenes, these individuals are usually able to compete athletically and to perform all types of heavy labor without symptoms. They may occasionally, however, manifest angina pectoris. When angina occurs with associated aortic regurgitation, it is often believed to be on the basis of poor coronary arterial perfusion secondary to the low diastolic resistance and of poor cardiac output. In other cases, coronary disease may be the cause. When left ventricular failure develops, the patient is said to have a life expectancy of around a year and a half. Medical treatment with the newer and more powerful diuretics has improved this prognosis somewhat. Dramatic change in the individual's prognosis, however, depends upon special surgical measures. Specifically, this entails ball-valve replacement.

Surgical treatment of aortic valve disease. The surgery for aortic stenosis has undergone a number of changes. Naturally, these changes imply the dissatisfaction with previous techniques. Historically, an early surgical approach to severe aortic stenosis was a sculpting procedure in which calcium was chipped from the involved aortic valve; structurally, a more pliable valvular state was said to have resulted from this form of surgery. It was unfortunate that often this calcific material was dislodged together with the other foreign material, bringing about embolism. Also, perforation of the remaining cusps often ensued, either as a direct result of instrumentation or because of superimposed bacterial endocarditis in the postoperative period.

A later step was to replace either the whole valve or portions of it with plastic Teflon and Ivalon cusps. These, however, had a tendency to become infected. The suture lines then disrupted, resulting in acute aortic regurgitation or intractable bacterial endocarditis. The result was a high incidence of late fatality. In a few instances this procedure had limited success.

In the past few years, prosthetic valves such as the Starr-Edwards valve have induced a resurgence of interest in ball-valve replacement for aortic stenosis and insufficiency.

The results in employing this valve for patients with aortic stenosis or regurgitation again indicate the marked differences between these two conditions. In patients having aortic stenosis, the diameter of the root of the aorta is smaller than it is in aortic regurgitation, for example. This necessitates working in a smaller space and creates the additional hazards of occluding one or more coronary ostia. Naturally, the size of the valve which can be placed in the aortic area is also of necessity limited (Figs. 6 and 7). This has meant that many patients who have successful valve replacement by this technique, for the

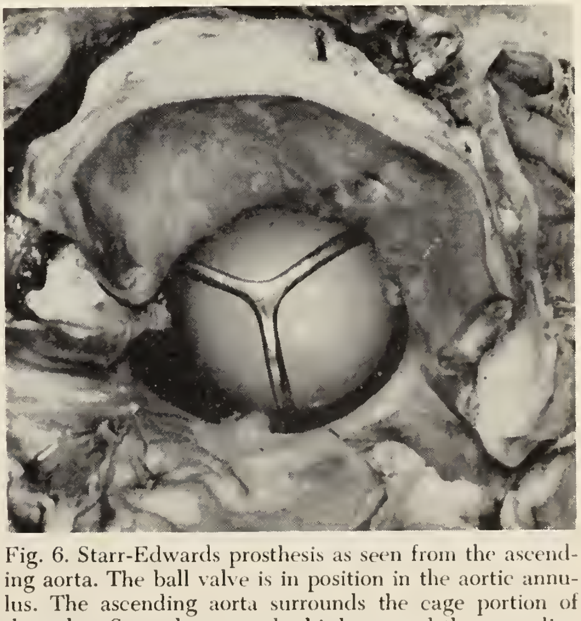

Fig. 6. Starr-Edwards prosthesis as seen from the ascending aorta. The ball valve is in position in the aortic annulus. The ascending aorta surrounds the cage portion of the valve. Space between the birdcage and the ascending aorta is limited.

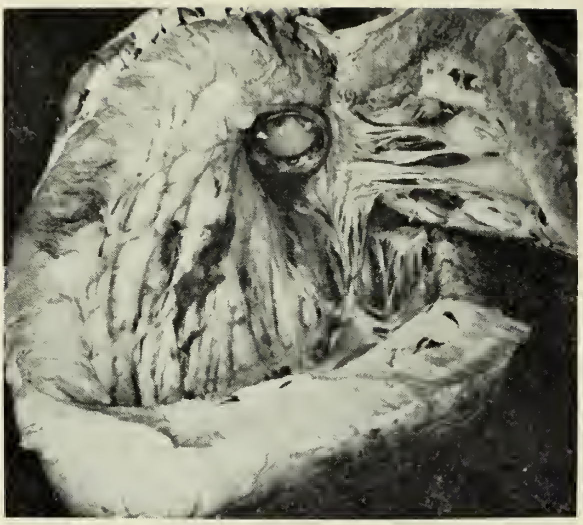

Fig. 7. The open left ventricle and outflow tract of the left ventricle, with a Starr-Edwards prosthesis in position in the aortic valve annulus. The orifice offered by this ball valve was not adequate to support normal circulation. A larger ball valve could not be positioned in this area. Mechanical aortic stenosis substituted for organic aortic stenosis in this case.

purpose of relieving aortic stenosis, have persistent mechanical stenosis secondary to the small aperture of the Starr-Edwards valve. Mechanical aortic stenosis has been substituted for an organic one. We have measured gradients across these prosthetic valves of up to 65 mm. Hg. Certainly, it would appear in many of these cases that a lesser degree of mechanical stenosis has been substituted for the original organic one.

Additionally, as the valve opens, blood spurts to the side of the ball, and the stream tends to be directed laterally against the ascending aortic wall rather than superiorly as it is in the anatomic one. It is possible that this rather uncommon direction of flow may create a Bernoulli effect at the ostia of the coronary arteries, creating jet lesions in the ascending aorta which may subsequently become infected, traumatizing the red cells unnecessarily. The complication of bacterial endocarditis of the ascending aorta in patients having ball-valve replacements of the aortic area is not uncommon. These valves also have a tendency to become thrombosed if anticoagulants are not employed. At the present time, the duration of anticoagulant treatment has not been determined.

In summary, the Starr-Edwards valve is a fairly good valve mechanically. It is, however, not the final answer to correction of aortic stenosis. The ideal valve would appear to be one in which the flow of blood occurs in a more physiologic manner, allowing more adequate orifice diameter.

One valve representing a trend in this direction is the Gott valve. This valve was developed by Dr. Vincent Gott of the Department of Surgery at the University of Wisconsin. It has been employed by surgeons at the University of Minnesota in a few instances with some satisfactory results. The valve is in the form of a butterfly or toilet seat, back to back (Fig. 8). The valve substance is plastic material which is impregnated with graphite. Graphite is said to repel clot formation, partly because it will adsorb heparin. Due to limited use and experience with this valve, it is not possible to predict its future.

Currently, another popular aortic valve in use is the Magovern valve (Fig. 9), which allows replacement in a matter of fifteen minutes to one-half hour instead of the usual one and one-half hours of cardiopulmonary bypass time. The valve very closely resembles the Starr-Edwards; however, it has teeth which come out of the bottom of the cage in a lateral direction. These teeth are extruded by rotating a handle which also serves to aid positioning the valve in the aortic root. The extruded teeth project through a layer of plastic used as a mesh for fibrin formation and then extend into the root of the aorta. No sutures are required, which greatly accelerates the operative procedure. Rarely, this valve will dislodge, causing acute aortic regurgitation. Currently, it has been the most successful in the hands of surgeons at the University of Minnesota Hospitals.

Direct current cardioversion for atrial fibrillation. One of the significant developments of the

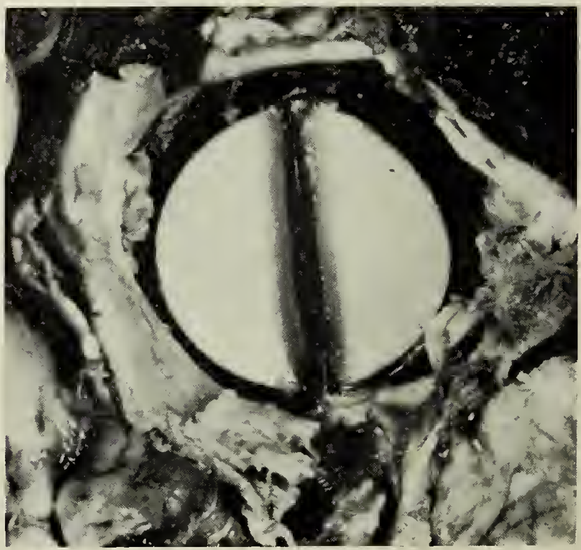

Fig. 8. The Gott valve, as seen from above, in position in the aortic annulus. The valve is butterfly in type with two synthetic leaflets which flap open on systole and close on diastole.

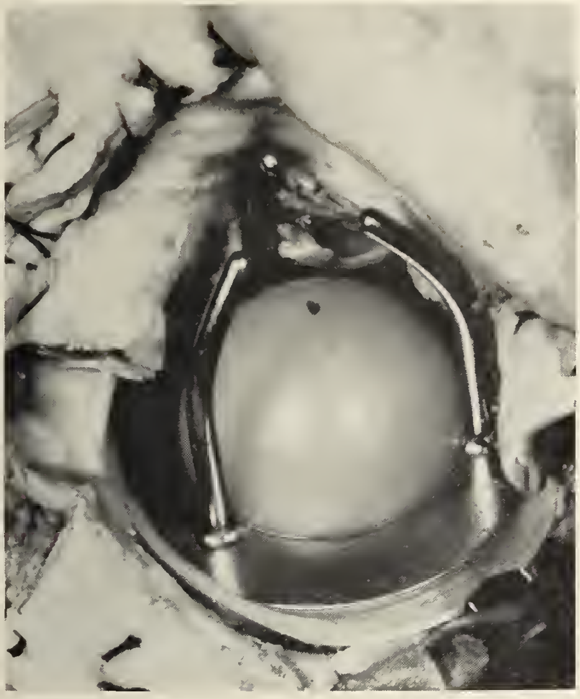

Fig. 9. The Magovern valve, as seen from above, in position in the aortic area. The valve is similar in many respects to the Starr-Edwards ball-valve prosthesis as it is birdcage in type. The apex of the birdcage, however, is open; crowding of the adjacent structures in the ascending aorta immediately superior to the aortic valve annulus is similar to that associated with the Starr-Edwards prosthesis. The valve has teeth which extend into the root of the aortic valve annulus, locking the valve in position after it has been properly positioned. The advantage of this valve is the reduced time required for positioning it, thereby reducing required cardiopulmonary bypass time.

last five years has been the technique of electrical conversion of chronic atrial fibrillation to normal sinus rhythm by DC current. This technique, which has been championed by Dr. Bernard Lown, has offered a very high incidence of initial conversion among patients with chronic atrial fibrillation. Although the duration of the maintenance of normal sinus rhythm is not yet known, there is little doubt that normal sinus rhythm has a very beneficial physiologic effect upon many individuals with rheumatic valvular disease.

It is often said that the selection of patients for cardioversion should be on the same basis as earlier techniques with quinidine or procainamide (Pronestyl®). Results are best in patients having atrial fibrillation of recent onset. Unfortunately, we often do not know the duration of atrial fibrillation in a given patient.

It has been our policy to place patients on anticoagulant treatment with warfarin sodium (Coumadin®) for a period of at least ten days before cardioversion. This has been done with the hope that fresh, friable thrombi would become firmly organized before conversion was attempted. Patients who have inordinately large left atria, ventricular conduction defects, or documented long-term (greater than two or three years) atrial fibrillation are probably not candidates for conversion.

We have noted a decrease in heart size up to 25%, after a period of two months, in individuals with mitral valve disease uncontrolled by other means who responded satisfactorily to DC cardioversion. When used with caution and with anticoagulants and with the premedication of Pronestyl® or quinidine, it can contribute significantly to the medical treatment of the complications of rheumatic valvular disease. Pronestyl® or quinidine should be indefinitely continued in maintenance doses to help prevent reversion of atrial fibrillation. In order to maintain the comfort of the patient, this procedure should be carried out with a form of general anesthesia.

SUMMARY

In the past decade, the treatment and understanding of rheumatic fever have improved considerably. The last few years have been marked by great strides in the development of suitable artificial heart valves for those who are already victims of rheumatic fever.

We look to the future for a continuing and improving control of rheumatic fever by programs such as the one now in existence in North Dakota. We also look for improvement in our diagnostic armamentarium, since one of our greatest needs at present is for a specific diagnostic test for acute rheumatic activity. We look forward to continuing advances in the use of surgical prosthetic valves and better means of cardiopulmonary bypass.

Also, we seek specific medical treatment for acute rheumatic fever. While these and other research efforts are under way, we look to our colleagues for cooperative and supportive efforts.

The author gratefully acknowledges assistance of Jesse E. Edwards, M.B., for use of pathologic specimens in his collection.

Supported by Research Grants HE 5694, HE 08940, and Training Grant 5 T1 HE 5570 of the National Heart Institute, National Institutes of Health, U.S. Public Health Service

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Introduction: Women in Medicine

J. ARTHUR MYERS, M.D.
Minneapolis

From the opening day of the first medical school in the United States at the University of Pennsylvania in 1765 until 1847 no woman had been admitted to a school of medicine. That year Elizabeth Blackwell, after having been rejected by 17 medical schools, was admitted to Geneva (later renamed Hobart) College at Geneva, New York. When President Benjamin Hale conferred the medical degree in 1849 she said, "I thank you, sir. It shall be the effort of my life, by God's blessing, to shed honor on this diploma." From the day of graduation on through her active life, Dr. Blackwell's accomplishments not only contributed significantly to the welfare of humanity but also encouraged and inspired young women to emulate her. "In a long and memorable career she founded the New York Infirmary for Women and Children and aided in the creation of the medical college there. She was the first woman admitted to the British Medical Register. She helped to found England's National Health Society, and in 1875 helped to found and then taught at the first college of medicine for women in England. She pioneered in preventive medicine and in the promotion of antisepsis and hygiene. She was responsible for the first chair of hygiene in any medical college."[1]

The medical world is deeply indebted to Hobart College for this first forward step destined to enlist young women in the program to benefit humanity everywhere. The Upper Midwest states are also deeply indebted to Hobart College for the fine training it provided young men who chose this area for their life's work. Augustine B. Hawley, after receiving the degree of Doctor of Medicine at Hobart in 1855, came to Red Wing and set up a private practice in 1857. One grandson, George M. B. Hawley II, is now a highly respected physician in Red Wing and another, John P. Hawley, Jr., a renowned industrialist in Minneapolis.

Soon after his arrival in Red Wing, Dr. Augustine Hawley was instrumental in bringing Reverend Edward P. Welles, his former roommate and a Hobart graduate, as first Rector of Christ's Episcopal Church. He became the first Episcopal bishop of Wisconsin in 1874.

On invitation of Dr. Hawley, Dr. C. N. Hewitt, another graduate of Hobart College, arrived in Red Wing in 1867. Hewitt became the father of public health in Minnesota.

Reverend George Leonard Chase, also a Hobart graduate, brought his wife to Minnesota seeking climatic benefit for her health in 1867. When the board of regents of the University of Minnesota was seeking its first president in 1868, Reverend Chase, Reverend Welles, Dr. Hawley, and Dr. Hewitt strongly recommended their friend and former Hobart schoolmate, William Watts Folwell, who became the first president in 1869.

In 1958 Hobart College established a Blackwell Award "to commemorate the life and works of Elizabeth Blackwell, Hobart alumna, M.D., 1849, first woman of the New World to graduate in medicine, the Elizabeth Blackwell Award is made annually to a woman in recognition of outstanding service to mankind."[1]

After it was announced that Elizabeth Blackwell had been admitted to the medical course and had won the degree of Doctor of Medicine at Geneva, there was a gradual letting down of the bars until now women are accepted in all medical schools. However, among the approximately 275,000 physicians in the United States today only about 17,000 are women.

In 1915 Dr. Bertha Van Hoosen founded the American Medical Woman's Association. Although the membership of this association consists of only approximately 5,000 physicians, special effort is in progress to increase the members during this fiftieth anniversary year.

Women in medicine have contributed magnanimously to maintenance and increase of the high standards of the profession. They are among

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J. ARTHUR MYERS *is with the School of Public Health and the Department of Medicine, University of Minnesota Medical and Graduate Schools.*

our best medical school teachers, investigators, and clinicians. They are doing brilliant work, not only in general practice but also in all specialties. Some of the finest physicians in the Upper Midwest states are women. This has been true since the first women physicians entered the area.

A woman who has contributed immensely to the health of the citizenry of this area is Dr. Ruth E. Boynton. In a profile published in the October 1964 issue of THE JOURNAL-LANCET, a former coworker, Dr. W. P. Shepard, included some of her finest contributions. This was the first of a Ruth E. Boynton Series of papers scheduled to appear from month to month. This series of articles, the remainder of which are all authored by women, has been arranged in recognition of Dr. Boynton's superb contributions. The authors are located throughout the entire nation. The published papers will demonstrate the wide variety of medical activities in which women are engaged and the superior quality of their work and accomplishments.

We are indebted to Dr. Evelyn E. Hartman and Dr. Catherine Corson West for their fine contributions in this issue. With much effort Dr. West has located the graduates in medicine of the University of Minnesota and provided a directory. This is a vital step toward organizing and inspiring group activities and also attracting larger numbers of young women to the medical profession.

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1. Official Publication, Hobart and William Smith Colleges, Vol. LXVIII, No. 3, August 1963.

GASTRIC FREEZE relieves pain immediately, but symptoms recur in about one-fourth of patients within six weeks and in two-thirds within six months. After a second freeze, symptoms recur in about half of patients within twenty-four weeks. Acid peptic secretion correlates closely with disappearance of pain but not with reappearance of symptoms. Data were obtained at six-week and three-, six-, and nine-month follow-up of 210 gastric freezes in 168 patients, 42 with a second freeze.

CLAUDE R. HITCHCOCK, M.D., JAMES E. BITTER, M.D., and R. DUNCAN SUTHERLAND, M.D., Hennepin County General Hospital, Minneapolis, Minnesota. Clinical evaluation of gastric freezing for duodenal ulcer. J. Amer. med. Ass. 188:409-414, 1964.

UMBILICAL HERNIAS usually develop within the first year of life and seldom occur for the first time after 5 years of age. The hernias are usually asymptomatic and most disappear by 10 years of age. During the first few weeks after birth, judicious elastic taping appears beneficial. Even though symptoms do not dictate surgical correction, this may be desirable to ease anxiety of parents and for cosmetic appearance. Such operations should be delayed until 18 months of age for boys and a year for girls.

HUGH B. LYNN, M.D., Mayo Clinic and Foundation, Rochester, Minn. Umbilical hernia. Ariz. Med. 21:253-255, 1964.

Health and Safety Needs in Children's Day Care Centers

EVELYN E. HARTMAN, M.D.
Minneapolis

GROUP DAY CARE CENTERS for preschool children are becoming increasingly more important because of the large numbers of mothers who are working outside of the home. Although licensing of these centers in Minnesota is a responsibility vested with the State Department of Public Welfare, local health departments must assume responsibility for prevention of outbreaks of communicable diseases in them, and for providing consultation on matters pertaining to health and sanitation.

The danger of exposure to infectious diseases in these centers is an ever present one and reports of such outbreaks over the years have made the need for surveillance and consultation by health agencies apparent.

In order to determine the overall situation in regard to health, sanitation, and safety in group day care centers for preschool children in Minneapolis, the City Health Department, with approval and cooperation from the Minnesota Department of Public Welfare, in 1963 conducted a survey of these centers, which included 22 for all-day care and 24 for half-day care. A grant from the Minnesota Department of Health to the maternal and child health program of the Minneapolis Health Department made such a study possible.

A part-time physician was hired to cooperate in planning and carrying out the project assisted by a Minneapolis Health Department sanitarian.

This report is an analysis of the findings in the 46 nurseries and nursery schools that were visited by the observers:

HEALTH RECORDS

The children's health records were found to be generally incomplete or inadequate. There was no uniformity as to content of information. Many of the children lacked up-to-date immunizations and tuberculin tests.

Teachers and other adults working with children frequently tended to be vague about their own physical examination or chest X-ray. This was particularly so in the half-day centers with their high numbers of mother volunteers and for the individuals who drove the buses or station wagons transporting the children.

HEALTH CARE AND SANITATION

Provisions to reduce the spread of infections within the nurseries were generally quite lax.

Although required in state standards only 13 of the centers had a daily health inspection of the children upon arrival. Isolation facilities were often haphazard. Many centers, although expecting the mother to come for a child who became ill during nursery hours, admitted this was not always feasible.

Most centers met the minimal state requirements of 1 toilet and 1 washbowl per 15 children. Those having less than the minimum were often centers operating only 2 or 3 mornings a week. One otherwise very good nursery was totally unacceptable in the toileting arrangement in that the children went completely away from the nursery area unescorted, with only some of the children washing their hands at a basin that had cold water. In this same nursery the children were using a stoppered sink in the kitchen for handwashing, all children using the same water.

A general lack of appreciation of the value of careful handwashing after toileting and before eating was evident. That is, even though children would be sent to wash their hands, teachers did

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EVELYN E. HARTMAN *is director, maternal and child health, Minneapolis Health Department.*

not make sure that they knew how to wash hands or that soap and running warm water were used. The average 3- or 4-year-old child needed considerably more time, help, and instruction in handwashing than most nurseries provided.

Further evidence of lack of understanding of how disease is spread within groups was found in the way the nurseries served food; in many of them, especially at snack time, the children helped themselves from common plates.

Dishwashing techniques were inadequate in the majority of the all-day care centers. Dishwashing was not a major problem in the half-day centers since all but 5 of them used paper service. If the hot water temperature for dishwashing is brought up to the recommended 170 to 180° F. in those nurseries that are not using paper service, a potential hazard of children scalding their hands will be created. In order to prevent this, the nurseries will need to install an automatic temperature control in the hot water line for lavatories or have separate hot water supplies for kitchen and washrooms.

General cleanliness was very good in all but 2 nursery schools.

Emergencies. There was a general lack of planning on the part of nursery directors for handling urgent emergencies. About half had releases from parents for the use of the designated nursery physician in such emergencies. Only a few of the remainder had a ready answer as to whom they would call and had posted telephone numbers for use in such an emergency.

First aid supplies. Most nursery directors were more than conscientious about their first aid supplies having, in addition to basic equipment such as gauze, adhesive tape and the like, an overabundance of proprietary antiseptics. When soap and warm running water are available and used proprietary antiseptics are generally unnecessary.

SAFETY HAZARDS

Fire safety. Despite a specific fire extinguisher requirement in the state standards for group day care centers, 13 of the nurseries had no extinguishers or had extinguishers that were out-of-date. Few nurseries were actively pursuing or planning fire drills. One had a fire drill plan which, when followed, revealed 1 locked exit and another exit barred by a desk. One center was using a cellar having only 1 exit which passed by an old furnace. Another center was operating on a second floor with only 1 stairway as an exit. Still another center had 2 exits from its very adequate second floor classrooms, but 1 of these exits was locked. One center had been visited by the fire marshal who called a surprise fire drill, causing much confusion.

Other types of hazards, most of which represented oversights on the part of the individual nurseries, included exposed electrical outlets and exposed hot radiators. One of the most serious oversights found was in an otherwise very good nursery school. In this school children were permitted to ride tricycles in the hallway. At one end of this hallway in the path of tricycle play was a full downward flight of stairs, guarded only by a flimsy folding gate with a very loose hook. In this same school, a teacher took 12 children across a busy parking lot in a disorganized and uncontrolled manner.

A couple of nursery schools transported children by putting as many as 10 to 12 children in 1 family type sedan. In one instance this was accomplished by having children sit on a platform across the back seat with other children sitting on the seat proper. This placed the children on the high platform in position to be thrown through the windshield in case of a sudden stop or collision. In 1 school 3- and 4-year-old children were transported by standard school bus with no adult helping them down the high steps.

Despite state requirements that an adult should be with the children at all times and that reasonable precautions must be taken for the safety of the children, there were a number of instances in which children had opportunities to explore potentially hazardous storage. For instance, children were left for as long as twenty minutes alone on the first floor of a home-centered nursery while the teacher helped other children take off their wraps in the basement. Within reach of the children on the first floor was storage containing knives, adult medications, various cleaning agents, and electrical equipment. In another instance, an unruly child was sent to stand alone out of sight of his teacher in an anteroom which opened to the laundry-furnace-tool room of the house.

RATING

On the basis of the above findings, an attempt was made to rate the day care centers for preschool children in Minneapolis. These ratings were based on subjective weighing of the findings for the individual centers as compared to each other, to state minimal standards for health and safety,[1] and to "ideal" standards established by consultation as well as from Child Welfare League of America sources.[2]

On a system of good, adequate, marginal, and poor, facilities of 7 centers were good, 21 were adequate, 16 marginal, and 2 poor. One of the poor schools would have been adequate except for the major fault of only 1 exit from a cellar playroom.

On the same system, the directors' comprehension and appreciation of health and safety factors as reflected in the school activities were also rated. Five were good, 32 adequate, 5 marginal, and 4 poor. The poor ratings reflect attitudes so permissive and relaxed that the observer could develop practically no feeling of having made any impression after interviewing and making recommendations to these directors.

Three schools were rated good in both respects and 4 schools were rated good in 1 respect and adequate in the other. One school was good in facilities and poor in comprehension.

DISCUSSION

The findings of the surveillance program substantiate the apprehensions that were felt in regard to deficiencies and problems existing in group day care facilities for children in Minneapolis regarding health, safety, and sanitation.

Reports of the visits and recommendations for correcting inadequacies were forwarded to the State Department of Public Welfare, which in turn used these reports for consultation with nursery directors. During the latter part of the year, a new procedure was initiated in that the health department observer at the time of the visit to the day care center reviewed her findings directly with the nursery director and made recommendations for improvement or commendations on good features. This new procedure made the inspection visits more meaningful by providing opportunities for health education. It also improved public relations by allaying some of the apprehensions of the nursery directors toward such an inspection. Health education materials including signs and symptoms of communicable diseases, health department regulations for communicable disease control, recommendations for up-to-date immunizations, a list of suggested first aid supplies and other materials were left at the time of the visit with the directors. Directors requesting specific help on equipment and items pertaining to sanitation were referred to the health department sanitarian.

As a further step to disseminate information, directors of the nurseries and nursery schools were invited to a meeting with representatives of the State Department of Public Welfare and the Minneapolis Health Department to discuss health problems that were of mutual concern. Assistance by the sanitarian was offered in technical matters relating to plumbing, dishwashers, and so forth.

At the time of this writing the Minnesota Department of Public Welfare is revising its standards for group day care and using many of our recommendations as a basis for health and sanitation requirements. (These standards have been amended effective 1965.)

SUMMARY

A survey was done by the Minneapolis Health Department in group day care centers for preschool children regarding health, sanitation, and safety. The findings substantiated the apprehensions that were felt in regard to potential health hazards. The inspection visits provided opportunity for health education and consultation to the nursery directors. Proposed revisions in state standards for health and sanitation in day care centers grew out of this study.

Population increases combined with employment of more young mothers will further increase the demand for day care for preschool children. In view of the findings of our study it would seem that local health departments cannot ignore their responsibility for the health and safety of these young children.

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Watching Women Graduate from Medical School, University of Minnesota

CATHERINE CORSON WEST, M.D.
Edina, Minnesota

THE SENIOR CLASS of 1965, University of Minnesota Medical School, included 10 women. Two of these ladies were elected to the honor society, Alpha Omega Alpha. They have a long legacy in their profession, as women physicians and as high scholastic achievers.

The first woman to graduate from a medical school in the New World was Elizabeth Blackwell, Geneva Medical School, western New York, at the head of her class on Jan. 23, 1849. By 1854 Dr. Aurora Giddings came to Minnesota —the first woman physician to practice in the state.

Not until 1884, thirty years later, did the University of Minnesota grant medical degrees. A faculty of 5 members had been appointed the year before by the board of regents, with the power to examine candidates and recommend those who seemed worthy to the board for the degree of Doctor of Medicine. In that first class of 1884, and those of 1885 and 1886, no woman graduated. Only 3 other classes since then have graduated without women (1890, 1911, and 1919).

In 1887 Catharine A. Burnes was the first woman to graduate from the University of Minnesota Medical School and she represented 50% of her class. This distinction has never been repeated.

No class graduated in 1888, but every year since (except the above mentioned years) has had from 1 to 18 women graduates. Actually, in 1943 there were 2 classes. During World War II classes were accelerated and one class graduated in March and the other in December 1943. Out of 222 graduates that year, 18 were women. Now in this year of 1965, the total number of women graduates has risen to 388.

Because of marriage these women present an extra problem for a record such as this. Some were married during medical school and continue to use their married names. Some were married after medical school and may or may not use their married names. In the directory that follows, really a graduation chronology, maiden and married names are recorded wherever they are known, though widowhood and the divorced state are not identified. Neither is it stated as to which name is used for professional purposes.

Concerning the year degrees were granted, it varies according to the policy of the medical school. From the beginning until 1918, the M.D. degree was granted. From 1918 to 1953 the M.B. degree was granted. After completion of a one-year internship or its equivalent, the M.D. degree was awarded. Since 1953 the M.D. degree has been granted upon graduation from the medical school without the internship requirement.

For purposes of this directory of Women Graduates of the University of Minnesota Medical School, the year of graduation is used. The degree granted that year is also listed.

Many of these "lady doctors" have lived longer than their male classmates, as is the pattern in the general population. In an American Medical Association News article, Aug. 3, 1965, it was pointed out that 21 M.D.s in the United States were 99 years of age or older, of which 5 were women. The oldest of the group was a woman physician—age 102.

According to this chronology of women graduates of the medical school, all of the 38 women who had graduated before 1900 are now deceased. The one who lived longest was Frances J. Henry, who died in 1961 at the age of 90. Now in 1965, out of the 388 graduates, 303 are living.

Most of them are practicing part-time if not full-time. Several have practiced for fifty years

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CATHERINE CORSON WEST *is a specialist in physical medicine and rehabilitation.*

or more. Many have married classmates and practiced together. One man married a classmate and after her death he chose as his second wife another classmate. One graduate, class of 1897, was followed by her daughter's graduation from medical school three years later, in 1900. Another mother-daughter combination was separated by twenty-five years (1914-1939), and still another separated by thirty-one years (1931-1962).

In the past seventy-eight years at least 5 pairs of sisters have graduated, including twins Bernette and Bernice Nelson, March 1943, who practiced together for several years. The Lampe sisters, Juliet, 1940, and Margaret, 1941, still practice together. The other sisters are the Moriarity's, Cecile, 1917 (d), and Berenice, 1926; the Ostergren's, Eva Jane, 1938, and Lenore, 1945; and the Jolly's, Elizabeth, 1946, and Ruth, 1947.

As for scholarship, hardly a year has passed without at least one woman being elected to the honor society, Alpha Omega Alpha. Upon graduation, the "top man of the class" has been a lady more than once. As do the men in medicine, the ladies scatter to all parts of the country. Internships, residencies, marriage, missionary work, and the armed services tend to disperse the classes. Only 96 of the 303 living women graduates of the University of Minnesota Medical School, excluding the 1965 class now in their internships, have remained in Minnesota.

An attempt has been made to make this "never-been-done-before" list as up-to-date as possible.

DIRECTORY

Class	*Degree*	*Name and address*
1887	M.D.	Burnes, Catharine A., Deceased
1888	No class graduated	
1889	M.D.	Carlson, Benedicta L., Deceased
1890	No women graduates	
1891	M.D.	Cutts, Mrs. Rollin E. (nee Smith), Deceased
	M.D.	McLoud, Mrs. Harriet (nee Conant), Deceased
1892	M.D.	Dight, Mary A. G., Deceased
	M.D.	Morrison, Alma E., Deceased
1893	M.D.	Aubin, Louise M., Deceased
	M.D.	Dietmeier, Mrs. Louise M. (nee Gerber), Deceased
	M.D.	Stephens, Edna A., Deceased
	M.D.	Young, Mrs. Esther H., Deceased
1894	M.D.	Baird, Mrs. James (nee Loretta J. Pettit), Deceased
	M.D.	Hughes, Mrs. Bertha, Deceased
	M.D.	Kirkpatrick, Mrs. Wm. D. (nee Addie F. Gilman), Deceased
	M.D.	True, Augusta I., Deceased
1895	M.D.	Bray, Mary E. (nee Bassett), Deceased
	M.D.	Haverfield, Addie R., Deceased
	M.D.	Koch, Margaret, Deceased
	M.D.	Nuzum, Helen B., Deceased
	M.D.	Pretlow, Clotilde L., Deceased
	M.D.	Rose, Mrs. Frances Eastman, Deceased
	M.D.	Terwilliger, Mrs. Innes L., Deceased
1896	M.D.	Hielscher, Mrs. Julian A. (nee Helen Hughes), Deceased
	M.D.	Hyde, Mrs. William T. (nee Rose Marie Merrill), Deceased
1897	M.D.	Bebb, Rose Anne, Deceased
	M.D.	Buell, Mary C., Deceased
	M.D.	Cahoon, Grace Wilson, Deceased
	M.D.	Granger, Mrs. George W. (nee Gertrude Baker), Deceased
	M.D.	Hall, Mrs. Andrea B. (nee Brauti), Deceased
	M.D.	Hurd, Mrs. Ethel E. (mother of Annah, 1900), Deceased
	M.D.	Keeney, Emma, Deceased
	M.D.	McClung, Alberta V., Deceased
	M.D.	Stahl, Harriet S., Deceased
1898	M.D.	Towers, Mary Elizabeth, Deceased
1899	M.D.	Agnew, Anna Marie, Deceased
	M.D.	Hall, Mrs. James O. (Charlotte C.), Deceased
	M.D.	Henry, Francis J., Deceased April 9, 1961
	M.D.	McClernan, Mrs. Bertha (nee Mackel), Deceased
	M.D.	McClung, Anna H., Deceased
1900	M.D.	Baker, Mrs. Marcy, Deceased
	M.D.	Hurd, Annah (daughter of Ethel, 1897), Deceased 1958
	M.D.	Kennedy, Jane F., Deceased 1962
	M.D.	LeVasseur, Irma, 681 Artillerie St., Quebec, Canada
	M.D.	Linton, Laura A., Deceased
	M.D.	Osborn, Lida, Deceased
	M.D.	Pratt, Mrs. Wm. J. (nee Charlotte P. Campbell), Deceased
1901	M.D.	Brandrup, Mrs. J. R. (nee Mary P. Hopkins), Deceased
	M.D.	Putnam, Catherine E., Deceased
	M.D.	Sweeting, Getta C., Deceased
	M.D.	Vallely, Rose, Deceased 1961
1902	M.D.	Barsness, Nellie O. N., 1562 N. Hamline Ave., St. Paul, Minn. 55113
	M.D.	Goodman, Minerva, 2255 Crofton Way, Stockton, Calif.
	M.D.	Hill, Eleanor J., Deceased
1903	M.D.	Fullerton, Ellen C., 2546 Fairmount, La Crescenta, Calif.
	M.D.	Helmuth, Kate Carlton, Deceased
	M.D.	Stickelberger, Josephine, Deceased 1962
	M.D.	Wilkinson, Stella L., Deceased 1955
1904	M.D.	MacKeen, Ida A., Deceased 1955
	M.D.	Nickerson, Margaret, Deceased
1905	M.D.	Griffin, Miriam E., Deceased 1952
1906	M.D.	Diessner, Mrs. Bertha G. (nee Newkirk, Mrs. H. D. Diessner, M.D.), Deceased 1957
	M.D.	Smith, Margaret I., 1929 W. 148th St., Gardena, Calif.
1907	M.D.	McMillan, Mary Ann (Mrs. H. B. Rodney), 1308 S. Brown, Spokane, Wash.
1908	M.D.	Alexander, Ida M., Deceased

Class	*Degree*	*Name and address*
1909	M.D.	Beede, Ethel R., Deceased
	M.D.	Ghostley, Mrs. Mary Chapman (later Mrs. Peterson), Deceased 1964
	M.D.	Stewart, Elsie G., Deceased
1910	M.D.	Grant, Kate Wyman, Deceased 1959
1911	No women graduates	
1912	M.D.	Hammons, Elizabeth M. Barnard, Deceased 1960
1913	M.D.	Bonness, Hazel, Deceased
	M.D.	Pearsall-Block, Phebe L., Deceased 1961
	M.D.	Warwick, Margaret (Mrs. Schley-McCullough) 610 Potomac Ave., Buffalo, N.Y. 14222
1914	M.D.	Hartig, Mrs. Hermina (nee Hermanson, mother of Marjorie, 1939) 4400 Park Ave., Minneapolis, Minn. 55407
	M.D.	Nye, Katherine A., 1357 Como Ave. W., St. Paul, Minn. 55113
1915	M.D.	Hansen, Olga S. (Mrs. J. C. Litzenberg), 3547 Girard Ave. S., Minneapolis, Minn. 55408
1916	M.D.	Boutelle, Louisa E., Deceased
	M.D.	Fullerton, Lynne A., Deceased 1959
1917	M.D.	Moriarity, Cecile R., Deceased 1963
	M.D.	Nutting, Clara Adams, Amherst, Mass.?
1918	M.B.	Holman, Nellie Pederson, Box 414, Melbourne, Fla.
	M.B.	Radusch, Frieda J., 919 Saint Cloud St., Rapid City, S.D.
1919	No women graduates	
1920	M.B.	Boynton, Ruth E., 13455 S.W. 75th Ct., Miami, Fla. 33156
	M.B.	Deane, Helen M., 1176 Aldrich St. N.E., Aiken, S.C.
	M.B.	Drips, Della G., 410 6th Ave. S.W., Apt. M5, Rochester, Minn. 55901
	M.B.	Ford, Frances Adelia, 2683 S. Lakeshore Rd., Applegate, Mich.
	M.B.	Kriz-Hettwer, Rose, 2527 E. Menlo Rd., Shorewood, Wis.
	M.B.	Mayer, Lillian M. (Mrs. Leo Fink), 6041 Zenith Ave. S., Edina, Minn. 55410
1921	M.B.	Diamond, Dorothy Sara, Albany, Ill.
	M.B.	Kepler, Mrs. Helen Mackeen, St. Charles, Minn.
	M.B.	King, Frances W. (Mrs. R. J. Salmon) 4928 Williston Rd., Minnetonka, Minn.
	M.B.	Scharff, Mrs. Fritz (nee Georgia DeJong) 6000 Oberlin Rd., Lorain, Ohio
1922	M.B.	Bohnsack, Eleanor (Mrs. Crim), 1405 17th Ave. S., Fargo, N.D.
	M.B.	Farnham, Mrs. Harriet (nee Bower), Deceased
	M.B.	Greisheimer, Esther M., 5450 Wissahickon Ave., Apt. 709A, Philadelphia, Pa. 19144
	M.B.	McLoon, Mary Anne, Deceased
	M.B.	Owens, Mrs. Irene N., Deceased
	M.B.	Pennington, Edna Scott, Midstate Medical Center, Nashville, Tenn.
1923	M.B.	Arthur, Frances Harding, 360 Herrontown Rd., Princeton, N.J. 08540
	M.B.	Backe, Irma A., Pentagon Building, Washington, D.C.
	M.B.	Carleton-Sparks, Rachel (Mrs. Keeton), Deceased
	M.B.	Corr, Magdalene Huchthausen (Mrs. Phil Corr), c/o Adolph Huchthausen, 173 Brentwood Park, 1100 Industrial Ave., Chula Vista, Calif.
	M.B.	Pryor, Helen Benton, 659 Middlefield Rd., Palo Alto, Calif.
	M.B.	Thelander, Hulda E., 40 Seafirth Pl., Tiburon, Calif.
1924	M.B.	Calvert, Charlotte Joslin, 109 Roby Rd., Madison, Wis.
	M.B.	Foot, Marynia L. (Mrs. Farnham), 243 E. 71st St., New York, N.Y.
	M.B.	Hilbert, Eunice (Mrs. MacNider Weatherby), 1314 Summit Ave., Minneapolis, Minn. 55405
	M.B.	Jennison, Janette H., Janesville, Minn.
	M.B.	Potter, Edith L. (Mrs. Meyer) Winter: 851 Estro Blvd., Ft. Myers Beach, Fla. Summer: Green Garden Township, Monee, Ill.
	M.B.	Willis, Elvira, Deceased
1925	M.B.	Fetter, Mary, 10042 N. 7th Pl., Phoenix, Ariz. 85020
	M.B.	Heck, Mrs. Frank J. (nee Ruth Vorhees), Deceased
	M.B.	Paul, Louise Mary (Mrs. Frank J. Heck), Wakefield, N.H.
	M.B.	West, Anne (Mrs. L. T. Robinson), Molly Stark Hospital, Box 367, Canton, Ohio
1926	M.B.	Bigler, Mary F. (Mrs. John Paul Ewing), Box 356, Chatsworth, Calif.
	M.B.	Couch, Mildred Warden, Deceased
	M.B.	Grimes, Marian (Mrs. Francis Collins), 730 Marquette Bank Building, Minneapolis, Minn. 55402
	M.B.	Kernkamp, Leila M., 502 N. Hairland St., Whittier, Calif.
	M.B.	Moriarity, M. Berenice, 63 Otis Ave., St. Paul, Minn. 55104
	M.B.	Nystrom, Ruth G., Deceased
	M.B.	Scholl, Marguerite J., Deceased
	M.B.	Whitman, Winifred Gray (Mrs. Merle Tuve), 135 Hesketh St., Chevy Chase, Md.
	M.B.	Winther, Nora M. C. (Mrs. C. H. Luethi), Columbus Athletic Club, Columbus, Ohio 43215
1927	M.B.	Browe, Evelyn L., Deceased 1959
	M.B.	Didriksen, Sarah H. (Mrs. Milton Rosekrans), 504 Hewett, Neillsville, Wis.
	M.B.	Fallon, Madeleine A., 2010 Wilshire Blvd., Los Angeles, Calif.
	M.B.	Keane, Mrs. J. C.
	M.B.	Keegan, Agnes M., 104 Sexton Building, Aberdeen, S.D.
	M.B.	Leggett, Elizabeth A., 525 W. Santa Clara Ave., Santa Anna, Calif.
	M.B.	Mayman, Evelyn W., 900 Brady Ave., Modesto, Calif.
	M.B.	Millbrook, May I., 1109 S. Lincoln, Urbana, Ill.
	M.B.	Rupp, Alice, 3161 Washington Blvd., Cleveland Heights, Ohio 44118
1928	M.B.	Alexander, Fay Knight, Lincolnville, Maine
	M.B.	Bowen, Sarah, 120 E. Marcy, Santa Fe, N.M.

Class	*Degree*	*Name and address*
	M.B.	Fischer, Viola I., Lutheran Clinic Selat Pagar, Lenggong, Upper Perak, Malaya
	M.B.	Howard, Laura Koon, 200 Retreat Ave., Hartford, Conn.
	M.B.	Johnson, Mrs. Olga (nee Holie), 302 5th St. S., Moorhead, Minn.
	M.B.	Shong, Geneva L. (Mrs. Rothemund), Orient State Institute, Orient, Ohio
1929	M.B.	Andersen, Leonora, 140 E. 54th St., New York, N.Y.
	M.B.	Gerdes, Maude M., Deceased 1959
	M.B.	Howard, Elna M., Box 570, Miles City, Mont.
	M.B.	Levine, Ida, (Mrs. Harry B. Reibstein), 34 Plaza St., Brooklyn, N.Y.
	M.B.	Riordan, Elsie M., 3007 Nicollet Ave., Minneapolis, Minn. 55408
	M.B.	Trommald, Gladys B. K., Deceased
1930	M.B.	Frary, Louise G.
	M.B.	Lynch, Helen M. (Mrs. Thor Bruce), City Health Dept. (Division School Health), St. Louis, Mo.
	M.B.	Murray, Elizabeth (nee Merrill), 106 W. 52nd St., Minneapolis, Minn. 55419
	M.B.	Richards, Marguerite P., 190 Hilltop Rd., San Francisco, Calif.
	M.B.	Walton, Mary, National Health Service, Washington, D.C.
	M.B.	Welch, Catherine B.
1931	M.B.	Fuller, Alice Harrison, 4500 Colfax Ave. S., Minneapolis, Minn. 55409
	M.B.	Ness, Claire Marie, 2050 E. 96th St., Cleveland, Ohio
	M.B.	Rasmussen, Ruth F. (Mrs. Rudolph Campbell), 18301 Douglas Rd., South Bend, Ind. 46637
	M.B.	Shaperman, Eva (Mrs. P. Gordon, mother of Harriet, 1962), 2215 Plymouth Ave. N., Minneapolis, Minn. 55411
	M.B.	Smeby, Sybil H., Deceased 1934
1932	M.B.	Conforth, Elizabeth L. (Mrs. H. G. Jackson), 2704 Glendower Ave., Los Angeles, Calif. 90027
	M.B.	Gaffney, Muriel, 5009 Tilden St. N.W., Washington, D.C.
	M.B.	Grytbak, Margit H., 1221 41st St. N., Seattle, Wash.
	M.B.	Haberer, Helen (nee Robertson, Mrs. Herman), Rt. 1, Box 123, Stacy, Minn. 55079
	M.B.	Helmick, Caroline E., 6028 Zenith Ave. S., Minneapolis, Minn. 55410
	M.B.	Karp, Mary, 250 E. Superior St., Chicago, Ill. 60611
	M.B.	Lundberg, Ruth I., 1991 W. Eldridge Ave., St. Paul, Minn. 55113
	M.B.	McGregor, Catherine G. (Mrs. G. W. Anderson), 4012 W. 48th St., Minneapolis, Minn. 55424
	M.B.	Petri, Karen Aileen, 4119 Montrose Blvd., Houston, Texas 77006
	M.B.	Thoreson, Bernice (nee Fegenshaw, Mrs. Albert Soldahl), 1619 Oakdale, St. Paul, Minn. 55118
	M.B.	Wulff, Marjorie (Mrs. Gradie Rountree), 70 Valley Rd., Louisville, Ky. 40204
1933	M.B.	Brockman, Helen (Mrs. John Barton), 812 E. 1st St., Independence, Iowa
	M.B.	Morrison, Charlotte J., 911 Medical Arts Building, Minneapolis, Minn. 55402
	M.B.	O'Brien, Veronica (Mrs. G. L. Orth), Grassland Hospital, Valhalla, N.Y.
	M.B.	Ripka, Emily (Mrs. Hautana), Deceased 1962
	M.B.	Spurzem, Clementine (Mrs. Tierney), 4425 S. 1st St., Arlington, Va.
1934	M.B.	Bailey, A. Margaret (nee Grandy), Veterans Administration Hospital, Minneapolis, Minn. 55417
	M.B.	Frear, Rosemary R., Route 2, Brooten, Minn.
	M.B.	Heathman, Lucy S. (Mrs. R. N. Barr), 1912 E. River Terrace, Minneapolis, Minn. 55414
	M.B.	Hoeger, Agnes M., American Lutheran Mission, Finschhafen, New Guinea
	M.B.	Iverson, Eleanor B. (Mrs. Fred Gunlaugson), 121 W. Elmwood Pl., Minneapolis, Minn. 55419
	M.B.	James, Harriet Dorothy, 1960 Commonwealth Ave., Boston, Mass. 02115
	M.B.	Johnson, Evelyn V. (Mrs. Frank Bock), 14021 N. Canterbury Dr., Phoenix, Ariz. 85023
	M.B.	Knights, Cathryn M. (Mrs. Oliver P. Jones), 23 Berkley Pl., Buffalo, N.Y. 14209
	M.B.	Oltman, Jane E. (Mrs. Samuel Friedman), Box W, Newton, Conn.
1935	M.B.	Anderson, Nina A. (Mrs. H. T. Atkins), 1212 Hershel Woods Lane, Cincinnati, Ohio 45226
	M.B.	McCree, Dorothybelle (Mrs. E. J. Kaufman), R. D. 3, Appleton, Minn. 56208
	M.B.	Olson, Lillian A., 1109 Minnesota, Bemidji, Minn. 56601
	M.B.	West, Mrs. Donald B. (nee Catherine Corson), 5301 Chantrey Rd., Edina, Minn. 55424
1936	M.B.	Bane, Helen W. (Mrs. H. W. Longfellow), 517 N. 5th St., Brainerd, Minn.
	M.B.	Lobb, Lois G., Patton State Hospital, Patton, Calif.
	M.B.	Mickelsen, Emma F. (Mrs. Emil Fronk), 4508 W. 44th St., Minneapolis, Minn. 55416
	M.B.	Smith-Vickers, Evelyn (Mrs. Harris), 200 15th Ave. E., Seattle, Wash. 98102
	M.B.	Thomas, Margaret Jane (Mrs. Charles E. McLennon), 701 Tennyson Ave., Palo Alto, Calif.
1937	M.B.	Becker, Arnetta M. (Mrs. Schuyler Brown), 11340 7th St. E., Treasure Island, Fla. 33706
	M.B.	Meller, Charlotte (Mrs. C. E. Biddle), Box 823, Auburn, Calif. 95603
1938	M.B.	Bergh, Solveig M., 6519 Nicollet Ave., Minneapolis, Minn. 55423
	M.B.	Boyden, Mary S., 330 Maine St., Lawrence, Kansas
	M.B.	Fraser, Betty M. (Mrs. Selverstone), Deceased 1964
	M.B.	Lambert, Lois R. (Mrs. J. E. Trow), 1540 E. Minnehaha Pkwy., Minneapolis, Minn. 55417

Class	*Degree*	*Name and address*
	M.B.	Ostergren-Larson, Eva Jane (Mrs. Bert Larson—see sister Lenore, 1945), 1239 Payne Ave., St. Paul, Minn. 55101
	M.B.	Schmidt, Mary A., P.O. Box 102, Hamilton, Mont.
1939	M.B.	Dahlstrom, Doris E. (Mrs. John C. Van Dalson), 723 S. Westredge Ave., Kalamazoo, Mich.
	M.B.	Gates, Emily H., University of Calif. Medical Center, Los Angeles, Calif. 90024
	M.B.	Hartig, Marjorie E. (Mrs. John Beer, see mother, 1914), 1665 Summit Ave., St. Paul, Minn. 55105
	M.B.	Hodgson, Jane E. (Mrs. Quattlebaum), 512 Lowry Medical Building, St. Paul, Minn. 55102
	M.B.	Kelly, Helen J., Deceased
	M.B.	Renning, Elsie L. (Mrs. J. W. Davies), 580 Park Ave., New York, N.Y. 10021
	M.B.	Sutton, Janet B., 113 E. Main St., Bartow, Fla.
1940	M.B.	Gregory, Harriet S. (Mrs. E. A. Bragg, Jr.), 17 Melby Rd., Attleboro, Mass.
	M.B.	Lampe, Juliet H., 545 New Moore Building, San Antonio, Tex. (See sister Margaret, 1941)
	M.B.	Lundgren, Olive A. (Mrs. J. G. Bateman), 5809 Corso Di Napoli, Long Beach, Calif. 90803
	M.B.	Mussey, Mary Elizabeth, 200 1st St. S.W., Rochester, Minn.
	M.B.	Olson, Ivy B. (Mrs. L. H. Heinz), 706 Sommerville, Shakopee, Minn.
	M.B.	Olson, Vendela E. (Mrs. W. C. Rucker), 308 Union St., Hackensack, N.J.
1941	M.B.	Botha, Eleanor (Mrs. T. J. Kennedy), 2455 S. Dahlia Lane, Denver, Colo.
	M.B.	Dahl, La Meta F., 1250 Saint Paul St., Denver, Colo. 80206
	M.B.	Gladitsch, Dorothea E., Country Club Circle, Brevard, N.C.
	M.B.	Lampe, Margaret R. (Mrs. W. R. Castle—see sister Juliet, 1940), 203 Tuxedo Dr., San Antonio, Tex. 78209
	M.B.	Todd, Ramona L., Napa State Hospital, Imola, Calif.
	M.B.	Wentink, Elaine (Mrs. J. C. Murphy), 4812 Ellicott St. N.W., Washington, D.C. 20016
1942	M.B.	Duerr, Eleanor, 361 Lowry Medical Arts Building, St. Paul, Minn. 55102
	M.B.	Galligan, Margaret D., 6900 Excelsior Blvd., Minneapolis, Minn. 55416
	M.B.	Geist, Susanne M. (Mrs. Black), 110 W. Harrison St., Dillon, S.C.
	M.B.	Jack, Laurine D., Veterans Administration Hospital, Jefferson Barracks, St. Louis, Mo. 63125
	M.B.	Nachtigal, Beatrice K., 110-20 71st Rd., Flushing, N.Y.
	M.B.	Stevenson, Margaret L., 1212 E. Main St., Alhambra, Calif.
March 1943	M.B.	Baird, Catherine (nee Carlson), University of California Hospital, Los Angeles, Calif. 90024
	M.B.	Bauer, Amelia (Mrs. Joseph Kahn), 106 Harrison Ave., Franklin, N. C.
	M.B.	Eilert, Mary Louise, 971 David Ave., Concord, Calif.
	M.B.	Johnson, Georgia (Mrs. Martin C. Olson), 4029 Elm Ave., Long Beach, Calif. 90807
	M.B.	Merrick, Charlotte (nee Teschan), 6 Ridge Rd., North Oaks, St. Paul, Minn. 55110
	M.B.	Nelson, Bernette (Mrs. Joseph Pellikka), 2961 Pine Ave., Slayton, Minn.
	M.B.	Nelson, Bernice (Mrs. J. R. Haley), 6215 5th Ave. S., Minneapolis, Minn. 55423
	M.B.	Pennington, Mary Helen, 1955 Kenwood Pkwy., Minneapolis, Minn. 55405
	M.B.	Rice, Roberta, Methodist Mission International, P.O. Box 1182, Seoul, Korea
	M.B.	St. Cyr, Betty (Mrs. John Gilson), 3 Prospect Way, Great Falls, Mont.
	M.B.	Troxil, Elizabeth, Veterans Administration Hospital, Minneapolis, Minn. 55417
December 1943	M.B.	Burns, Catherine (Mrs. Clifford Lusk), R.D. 2, Box 242-A, Excelsior, Minn.
	M.B.	Gamble, Alice H. (Mrs. O. W. Beard), 7008 Rockwell Rd., Little Rock, Ark.
	M.B.	Holland-Moritz, Mrs. E. K. (nee Roxie Mudgett), 2920 Valley Dr., Ann Arbor, Mich.
	M.B.	Knudsen, Helen L., 2101 E. River Rd., Minneapolis, Minn. 55414
	M.B.	Seebach, Lydia (Mrs. Keith Wentz), 2813 Scott St., San Francisco, Calif.
	M.B.	Swain, Jean, 491 Luther Dr., Santa Clara, Calif.
	M.B.	Templeton, Helene, 1424 4th Ave., Seattle, Wash. 98101
1944	M.B.	Darling, Alice (Mrs. Joseph Jorgens), 176 Taylor Ave., Fort Snelling, Minn.
	M.B.	Dowell, Margaret (Mrs. Arthur Gravatt), 307 South Corl St., Apt. 5, State College, Pa.
	M.B.	Hauser, Elizabeth (Mrs. Bureh), 2012 43rd Ave. E., Seattle, Wash.
	M.B.	McGrew, Elizabeth A., 548 Judson Ave., Evanston, Ill.
	M.B.	Moren, Adelaide (Mrs. E. T. Cedarleaf, Jr.), 3300 Arcwood Rd., St. Paul, Minn.
	M.B.	Taylor, Mrs. Donald (nee Gloria Ann Griffin), 233 A St., San Diego, Calif.
	M.B.	Tichy, Fae Y., 960 E. Green St., Pasadena, Calif.
	M.B.	Vivino, Mrs. Earl (nee Jean Jermsta), 7219 Honeywell Lane, Bethesda, Md.
1945	M.B.	Craig, Mary Elizabeth (Mrs. H. W. Lincoln), 3400 Dakota Ave., Minneapolis, Minn. 55416
	M.B.	Eckles, Nylene (Mrs. A. Kirschbaum), M.D. Anderson Hospital Institute, Houston, Texas 77025
	M.B.	Eldred, Ruth (Mrs. Ward Smathers), 18741 Roseland St., Lathrup Village, Mich.
	M.B.	Nimlos, Mrs. K. O. (nee Lenore Ostergren), 762 Labore Rd., St. Paul, Minn. 55117 (see sister Eva Jane, 1938)

Class	*Degree*	*Name and address*
March 1946	M.B.	Erickson, Ethel E., 2002 Holcombe Blvd., Houston, Texas
	M.B.	Gumprecht, Mrs. Donald M. (nee Jane Doering), 302 N. 5th, Coeur d'Alene, Idaho
	M.B.	Jensen, Mary Jane (Mrs. Sherman-McNaul), 7512 Delaforge Dr., San Jose, Calif.
	M.B.	Stevenson, Helen (nee Peik, Mrs. J. C. Dahl), Student Health Service, University of Minnesota, Minneapolis, Minn. 55414
December 1946	M.B.	Adcock, Madeline S., 1394 Goodrich Ave., St. Paul, Minn. 55105
	M.B.	Brey, Theresa (Mrs. F. J. Haddy), 633 Culbertson Dr., Oklahoma City, Okla. 73105
	M.B.	Eil, Lois L., 77 Puritan Ave., Yonkers, N.Y.
	M.B.	Follansbee, Roberta (Mrs. R. V. Bergstrom), 3050 Monmouth Rd., Cleveland Heights, Ohio 44118
	M.B.	Furman, Christine (Mrs. David Webster), 6845 Pillsbury Ave., Minneapolis, Minn. 55423
	M.B.	Jolly, Elizabeth Ann (see sister Ruth, 1947), Box 871, Martinez, Calif.
	M.B.	McKenzie, Eva Elaine (Mrs. Roy R.), 8 N. Mallard Rd., St. Paul, Minn. 55110
	M.B.	Taylor, Maxine Y.
1947	M.B.	Bouthilet, Florence (Mrs. Kenneth B. Fick), 2241 St. Clair Ave., St. Paul, Minn.
	M.B.	Cedarleaf, Cherry B., 814 Mahtomedi Ave., Mahtomedi, Minn.
	M.B.	Cottor, Anne (Mrs. Robert Kuhn), 4203 W. 13 Mile, Royal Oak, Mich.
	M.B.	Jolly, Ruth M. (Mrs. Hauck, see sister Elizabeth Ann, 1946), 15000 Foothill Blvd., San Leandro, Calif.
	M.B.	Martin, Doreen A., Pepin, Wisconsin
	M.B.	Teberg, Mary (Mrs. Scallen), 110 W. Elmwood Pl., Minneapolis, Minn. 55419
1948	M.B.	Aronow, Regine A. (Mrs. Hoag), 501 Washington Rd., Grosse Pointe, Mich.
	M.B.	Bockelheide, Priscilla A., 1700 Esplanade, Chico, Calif.
	M.B.	Dahl, Jeanne (Mrs. E. J. Diefenbach, Jr.), 5933 Halifax Ave. S., Minneapolis, Minn. 55424
	M.B.	Edwards, Laura E., Baptist Mission, Harisinga Darrang, Assam, India
	M.B.	Engstrom, Ruby M., 22148 Michigan Ave., Dearborn, Mich.
	M.B.	Hoilund, Lucille J., Jackson Hall, University of Minnesota, Minneapolis, Minn. 55414
	M.B.	Lowry, Jeanette E. (Mrs. Kraemer), 950 Medical Arts Building, Minneapolis, Minn. 55402
	M.B.	McCabe, Margaret (Mrs. John E. Gartland), 180 E. Delaware Pl., Chicago, Ill. 60611
	M.B.	Safford, Helen M., 499 5th St., Oakland, Calif. 94607
	M.B.	Thornton, Mary
	M.B.	Virnig, Hildegard J., Caledonia, Minn.
	M.B.	Wong, Gloria (Mrs. Chung), 943 Union St., Brooklyn, N.Y. 11215
1949	M.B.	Agnew, Suzanne (Mrs. G. G. Snively), 2315 Stockton Blvd., Sacramento, Calif. 95817
	M.B.	Colle, Eleanor, 954 Dunsmuir Rd., Mount Royal, Quebec, Canada
	M.B.	Grant, Suzanne, 6519 Nicollet Ave., Minneapolis, Minn. 55423
	M.B.	Hacker, Elaine M., 19557 Mack, Detroit, Mich. 48236
	M.B.	Huelskamp, Margaret M., 950 The Alameda, San Jose, Calif. 95126
	M.B.	Jarvis, Mrs. B. W. (nee Marilyn Anderson), 27 Citadel Rd., Morgantown, W. Va. 26401
	M.B.	Johnson, Delores E., 1000 W. Carson St., Torrance, Calif.
	M.B.	McGaffey, Hazel L., 921 N.E. 13th St., Oklahoma City, Okla. 73104
	M.B.	McKenna, Elizabeth M., 5075 Mission Blvd., San Diego, Calif. 92109
	M.B.	Nelson, Maxine O., 730 Chicago Ave., Minneapolis, Minn. 55415
	M.B.	Novick, Rosalind, 2021 Genceres Dr., New Orleans, La. 70123
	M.B.	Rosander, Phyllis E., Deceased 1955
	M.B.	Wong, Lillian, 49 4th St., San Francisco, Calif. 94103
1950	M.B.	Filante, Margaret S., 710 C St., San Rafael, Calif.
	M.B.	Funke, Joyce L., 1276 Bayard Ave., St. Paul, Minn. 55116
	M.B.	Gault, Sarah (nee Dickie, Mrs. N. L. Gault, Jr.), 1595 Vincent St., St. Paul, Minn. 55108
	M.B.	Lund, Naomi G., 3021 N. Oakland Ave., Decatur, Ill.
1951	M.B.	Adler, Shirley (Mrs. Glenn Howard), 2703 S. Gaffey, San Pedro, Calif.
	M.B.	Cedarleaf, Shirley J., 2405 1st Ave. S., Minneapolis, Minn. 55404
	M.B.	Goepfert, Mary, Veterans Administration Hospital, Oklahoma City, Okla. 73104
	M.B.	Hanson, Mildred (nee Schaffer), 5529 Woodlawn Blvd., Minneapolis, Minn. 55417
	M.B.	Hochstetler, Sarah K., Presbyterian Medical Center, San Francisco, Calif. 94115
	M.B.	Knutson, Donna M. (Mrs. Ward Edwards), 3545 Glenhurst, Minneapolis, Minn. 55416
	M.B.	Teberg, Annabel J., 1894 N. Euclid Ave., Upland, Calif.
	M.B.	Visscher, Barbara R. (Mrs. F. H. Kahn), 3309 Corinth Ave., Los Angeles, Calif. 90066
1952	M.B.	Gilbertson, A. Sigrid, Nicollet Clinic, 2001 Blaisdell Ave., Minneapolis, Minn. 55404
	M.B.	Johnson, Carolyn (Mrs. C. R. Wesenberg), 1316 Keston St., St. Paul, Minn. 55108
	M.B.	Nelson, Wilhma (nee Bowman), Route 4, Box 406 N., Albany, Oregon
	M.B.	Schaffhausen, Mildred (Mrs. Irwin F.), 400 W. 66th St., Minneapolis, Minn. 55423
	M.B.	Smith, Nadine (Mrs. A. W. Ide, Jr.), 541 Turnpike Rd., Minneapolis, Minn. 55416

Class	*Degree*	*Name and address*
1953	M.D.	Arneson, Genevieve A., 1502 Weyer St., New Orleans, La.
	M.D.	Besser, Vera (Mrs. Fryling), 425 Hazelwood Ave., San Francisco, Calif.
	M.D.	Bilzens, Mrs. Karlis (nee Valija Skaidrite), 3015 Stephenson Pl. N.W., Washington, D.C.
	M.D.	Brown, Phyllis (nee White), Deceased
	M.D.	Countryman, Ethlyn (Mrs. P. E. Jackson), 1548 Ardenwood Dr., San Jose, Calif.
	M.D.	Leinonen, Wendla (Mrs. Neil Macheledt), 720 River Lane, Anoka, Minn.
	M.D.	Sundberg, R. Dorothy, 6120 Zenith Ave. S., Minneapolis, Minn. 55410
	M.D.	Ure, Barbara, 119 E. 84th St., New York, N.Y. 10028
1954	M.D.	Anderson, Eunice (Mrs. Davis, 1118 18th St., Bismarck, N.D.
	M.D.	Carlin, Jean E., 6510 E. Spring St., Long Beach, Calif. 90815
	M.D.	Cook, Mrs. J. J. (nee Carol Lynn), 787 Kirkcrest Rd., Danville, Calif.
	M.D.	Decker, Kathleen (nee Hogan), Deceased 1961
	M.D.	Hiduchenko, Katherine F., Newark, New Jersey
	M.D.	Jacklin, Mrs. Alexander (nee Lucille Saloum), 1017 E. 1st St., Duluth, Minn.
	M.D.	Larsen, Martha C., 329 E. 68th St., New York, N.Y. 10021
	M.D.	Larson, Dorette (nee Wheat), P.O. 157, State Hospital, Fergus Falls, Minn.
	M.D.	Paulsen, Mrs. Monrad G. (nee Elsa Proehl), 430 W. 116th St., New York, N.Y. 10027
	M.D.	Schoon, Doris V., 9531 Colchester Dr., Anaheim, Calif.
1955	M.D.	Berzina, Ligita G. (Mrs. Moettus), 26915 Westwood Rd., Westlake, Ohio
	M.D.	Subak, Barbara J. (nee Hanson, Mrs. Nick S. Subak), 3501 Stinson Blvd., Minneapolis, Minn. 55418
	M.D.	Vaubel, Carol (nee Vilen, Mrs. Lawrence Vaubel) 4321 York Ave. S., Minneapolis, Minn. 55410
1956	M.D.	Blochowiak, Beverly Jean, 3341 S. 54th St., Milwaukee, Wis.
	M.D.	Covert, Jean F. L. (Mrs. Sauer), St. Peter State Hospital, Pouch A, St. Peter, Minn.
	M.D.	Goodman, Mrs. Malka L. (Mrs. Ernest Goodman), 1864 Pinehurst St., St. Paul, Minn. 55116
	M.D.	Halling, Donna Jean (Mrs. Larson), 7404 W. Wedgwood St., Milwaukee, Wis. 53220
	M.D.	Kosiak, Irene (Mrs. A. J. Perpich), 335 Chestnut St., Virginia, Minn.
	M.D.	Robinson, Margaret G. (Mrs. Gordon LaFlash), 246 77th St., Brooklyn, N.Y. 11209
1957	M.D.	Balian, Lucy J. (Mrs. R. R. Rorke), 120 Chestnut St., Moorestown, N.J. 08057
	M.D.	Bergstrom, LaVonne B., Box 317, San Luis, Colo.
	M.D.	Johnson, Doris Irene, 661 W. 1st St., Tustin, Calif.
	M.D.	Toussaint, Florence A., 844 Trenton Dr., Sunnyvale, Calif.
1958	M.D.	Frantz, Marthella J., Maumee Valley Hospital, Toledo, Ohio 43609
	M.D.	Naumann, Miriam K. (Mrs. Charles McCreary), Wandoor, Kerala, India
	M.D.	Painter, LaVonne M.
	M.D.	Rosine, Barbara A. (Mrs. Bordan), 1414 Payne Ave., St. Paul, Minn. 55106
	M.D.	Vitols, Eugenie, 3490 20th St., San Francisco, Calif.
1959	M.D.	Blumentals, Ausma S. (Mrs. Janis), 973 Bradley St., St. Paul, Minn. 55101
	M.D.	Flory, Mrs. W. D. (nee Sonja K. Myhre), 1822 Ardmore Rd., Columbia, S. C. 29206
	M.D.	Hill, Charlotte W., 209 N. McCarrons Blvd., St. Paul, Minn.
	M.D.	Kelly, Helen M., 372 W. Moreland, St. Paul, Minn.
	M.D.	Puumala, Mrs. R. R. (nee Barbara Meyer), 307 Dalewood Ave., Cloquet, Minn.
	M.D.	Smith, Darline Donalda, Veterans Administration, Oakland, Calif. 94612
1960	M.D.	Haaland, Elizabeth M. (Mrs. Johnson), 1117 Arbita Court, Madison, Wis.
	M.D.	Lansky, Mrs. Lester (nee Shirley Bean), University Hospitals, Pediatrics Resident, Minneapolis, Minn. 55414
	M.D.	Olson, Mrs. R. E. (nee Barbara Ford), 1568 Charlton St., St. Paul, Minn. 55118
	M.D.	Oseid, Betty J. (Mrs. M. E. Carey), 235 Bedford St. S.E., Minneapolis, Minn. 55414
1961	M.D.	Engeset, Nancy Jo, Univ. of Pa. Hospital, Philadelphia, Pa. 19104
	M.D.	Myers, Leah Terese, St. Elizabeth's Hospital, Boston, Mass. 02135
	M.D.	Olness, Karen (Mrs. Hakon D. Torjesen), 2022 Pierce Mill Rd. N.W., Washington, D.C. 20010
	M.D.	Wieseke, Neva M., Casilla 2492, Lima, Peru
1962	M.D.	Anselment, Lois, 233 School Ave., Excelsior, Minn.
	M.D.	Cloutier, Joan E., Union Memorial Hospital, Baltimore, Md.
	M.D.	Fremland, Mrs. Alan (nee Harriet Gordon, see mother, 1931), 2885 Kobe Dr., San Diego, Calif. 92123
	M.D.	Gökcen, Barbara (nee Williamson), 1231 Wills Pl., Minneapolis, Minn. 55422
	M.D.	Grunnet, Margaret, 3944 Pine St., Philadelphia, Pa. 19104
	M.D.	Hobday, Mrs. H. Thomas (nee Kathleen Flanagan), P.H.S. Health Center, Chinle, Ariz. 86503
	M.D.	Howell, Mary (Mrs. A. Ervin), 4 Windsor St., Haverhill, Mass.
	M.D.	Kohler, Mrs. Peter (nee Rosemary Eckert), 709 Delaware St., Minneapolis, Minn. 554514
	M.D.	Lund, Nancy Ruth, 2033 S. State, Box 54, Salt Lake City, Utah 84115
	M.D.	Norseen, Phillicent, Kaiser Foundation, San Francisco, Calif.
1963	M.D.	Ahlquist, Mary G. (Mrs. Robertson), Deceased 1965

Class	*Degree*	*Name and address*
	M.D.	Crutchfield, Mrs. Chas. (nee Susan Ellis), 4548 Oakland Ave. S., Minneapolis, Minn. 55407
	M.D.	Hallquist, Beverly M., Hillside Hospital, Glen Oaks, N.Y.
	M.D.	Lindquist, Janet M., Pediatrics Resident, Philadelphia General, Philadelphia, Pa.
	M.D.	Rieke, Alyson, Kaiser Hospital, San Francisco, Calif.
	M.D.	Ryan, Patty J., 217 28th and Como S.E., Minneapolis, Minn. 55414
1964	M.D.	Peake, Zanna, Lutheran Hospital, La-Crosse, Wis.
	M.D.	Wester, Mrs. D. R. (nee Mary Sue Heibert), Bethesda Lutheran Hospital, St. Paul, Minn.
1965	M.D.	Belgea, Kathy, Wisconsin University Hospitals, Madison, Wis.
	M.D.	Bjork, Darla, King's County N.Y., 451 Clarkson, Brooklyn, N.Y. 11203
	M.D.	Granquist, Judy, Cook County, Chicago, Ill.
	M.D.	Hyvarinen, Marcia, Bethesda Lutheran Hospital, St. Paul, Minn.
	M.D.	Larson, Carol Ann, Ancker Hospital, St. Paul, Minn.
	M.D.	Lorber, Ruth, Syracuse Upstate Medical Center, Syracuse, N.Y.
	M.D.	MacNab, Betty Jane, St. Francis Hospital, Honolulu, Hawaii
	M.D.	McManus, Marilyn, Herrick Memorial Hospital, Berkeley, Calif.
	M.D.	Nelson, Audrey, N.C. Memorial Hospital, Chapel Hill, N.C.
	M.D.	Pajari, Karen, University of Kansas Medical Center, Kansas City, Kans.

SURGERY for carefully selected cases of solitary pulmonary metastatic cancer has given good results. Pulmonary metastasis often occurs after removal of tumors of the rectum and left colon, breast, kidney, and skin. The metastatic lesion usually develops in peripheral lung parenchyma. The tumor appears as an uncalcified coin-type shadow in thoracic roentgenograms, the most valuable means of diagnosis. Before operation is decided upon, previous records must indicate that the primary tumor has been completely removed, recurrence or metastasis other than the pulmonary lesion must not be found, and age and condition of the patient must justify the procedure. Treatment of choice is lobectomy or segmental resection; pneumonectomy usually is not necessary. During 1941-59, 169 resections for solitary metastatic lung lesions were performed in 165 patients, with a five-year survival rate of 31%.

O. THERON CLAGETT, M.D., and LEWIS B. WOOLNER, M.D., Mayo Clinic and Foundation, Rochester, Minn. Surgical treatment of solitary metastatic pulmonary lesion. Med. Clin. N. Amer. 48:939-943, 1964.

DAMAGE OF CERVICAL LIGAMENTS in the nuchal region can occur by attrition without associated neck injury. Recognition of effects of aging on interspinous nuchal ligaments is important in personal injury claims following automobile accidents. The nuchal region in 35 postmortem subjects 6 to 98 years old was dissected; pathological change in ligaments was evident in 29, although only 3 died of causes related to neck injury and 3 others had had transitory neck discomfort.

D. ROSS HALLIDAY, M.D., C. ROGER SULLIVAN, M.D., W. HENRY HOLLINSHEAD, PH.D., and ROBERT C. BAHN, M.D., Mayo Clinic and Foundation, Rochester, Minn. Torn cervical ligaments: Necropsy examination of the normal cervical region of the spinal column. J. Trauma 4:219-232, 1964.

Bernard J. Gallagher, M.D.

1889-1962

WILLIAM BERNARD GALLAGHER, M.D.
LaCrosse, Wisconsin

MARGARET GALLAGHER SPOO
Rochester, Minnesota

Ben Gallagher of Waseca, Minnesota, was a physician and surgeon in general practice for forty-one years, primarily in his hometown. He was an excellent doctor in whom compassion was a hallmark. In the course of his lifetime he found "the serenity to accept the things I cannot change, courage to change the things I can, and wisdom to know the difference."

As a young doctor, just finished with his internship, he served in 1917-1918 as a battalion medical officer with the 2/4th and 2/5th Gloucester battalions in the British Army in France. He returned home in 1919 and during the next fifteen months, while on a fellowship at the Mayo Clinic, he wrote an account of his war experiences. Then he put it away in his footlocker where it remained for forty-four years. In June 1965, *American Heritage* magazine published excerpts from this manuscript under the title "A Yank in the B.E.F."

In 1965, forty-seven years after the events he had described, survivors of the Gloucesters remember him well. Oswald Bradley, Gallagher's former medical orderly, writes:

> He treated me as a friend. He was one of the finest officers one could wish to work with. He had no fear of enemy shelling, his first thought always was for the men. I feel it an honour to have worked with him. When we were in our advanced aid post he would always be thinking of the men in the fighting line and when the wounded and sick came through our hands (and I can assure you they were many) nothing was too much trouble to him. He gave them every care and comfort it was possible to give. His motto was certainly Service not Self. He could have gotten away but he refused to leave the wounded. How he must have been loved by his many patients in his own practice on his return to the U.S.A.

Former Maj. G. L. Day of the Gloucesters writes:

> Everyone in the battalion liked him. At Marcelcave he was attending the wounded and very courageously would not leave them.

Former Sgt. J. H. Gurney of the Gloucesters writes:

> Lt. Gallagher's total service with us extended for a proportionately short time (five months)—but the fact that an American Medical Officer had joined us was enough to make him a special personality amongst the 2/5th Gloucesters. It was somewhat mysterious to us young soldiers, who were ignorant of high policy, that an American Medical Officer should be posted to us. He was extremely well liked by the men, and not only that, he showed most sympathy and understanding in his dealing with them. And obviously, he was very brave. He must have been courageous to be in the van of our American cousins to come over to join us as Allies in

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WILLIAM BERNARD GALLAGHER *is with the Skemp Clinic in LaCrosse, Wisconsin, and* MARGARET GALLAGHER SPOO *lives in Rochester, Minnesota.*

> that Great War. He showed great gallantry and devotion to duty in remaining at his medical post, although overwhelmed by attacking forces. In his professional and medical capacity he regarded mankind with a common bond of union and treated them accordingly.

These observations from men who had not seen him since 1918, with whom he had served a relatively brief period, underline the essence of the man—as he was then and as he remained.

Ben Gallagher was born on a farm in Wilton Township in southern Minnesota but grew up in nearby Waseca as part of a close-knit family consisting of his parents, Bernard and Katherine, four brothers, Henry, Frank, Bob, and Joe, and a sister, Rosella (Mrs. John Cunningham). His dad, "Ber" Gallagher, worked in a lumber yard. According to Ben, he was best known as the one who spent two years in the first grade. Since the nuns in the parochial school would not teach boys after the sixth grade, they transferred at that level to the public school from which Ben graduated in 1908.

To earn money for college he went to work at the local flour mill for $20 a month, and also learned to be a telegrapher. Waseca was a railroad town and Ben, like many young boys, followed the comings and goings of the daily trains and hung around the edges of the work going on in the roundhouse. He was to remain a railroad buff all of his life. Baseball also absorbed him. The Gallaghers were avid ball players and Ben was described as a smart, tough little pitcher, making up in guile and control what he lacked in brawn. He toyed for a time with the idea of trying out for the major leagues.

His older brothers, Henry and Frank, became lawyers and his younger brother, Bob, became a dentist. Ben, in 1910, enrolled in the University of Minnesota to study medicine. He graduated from the medical school in 1916.

He was finishing his internship at the Minneapolis City Hospital when the United States entered World War I in 1917. He applied for a commission as a medical officer and requested active duty. He was ordered to Washington, there assigned immediately to the British Army and sent to England. By 1917 the British were desperately short of medical officers. The life expectancy of a battalion medical officer on the Somme in France was said to be eleven days. When America entered the war England's first request was "Send us doctors." Ultimately some thirteen hundred were sent but when Gallagher and his group arrived in England they were something of a curiosity because they were the first Americans many Englishmen had ever seen.

After six weeks' work at Graylingwell War Hospital, a large British general hospital in Chichester in the south of England, Gallagher and some of the other Americans were ordered to France. On arrival there, in late November 1917, the Americans were separated and assigned to various British divisions up and down the front. It was to be many months before Gallagher saw another American. He was sent to Arras, to the ambulance company of the 61st Division. After a short time he went into the line to replace a friend, killed the previous day. He reached the headquarters dugout of the Gloucester battalion in the ruined village of La Vacquerie, on the Cambrai front, just as the Germans attacked. "I was going 'over the top' backwards behind a German barrage," he wrote later. It was quite an introduction to combat for a man with scarcely any military training. As the fighting raged on Gallagher pitched in with an English doctor from another battalion. He wrote later:

> Through that day and night a dug-out we used as an aid-post was jammed all the time. Men lay on the floor and suffered the agonies of a living death with the most frightful wounds. We would look at the men in the trenches and decide which should be brought down and which were so badly wounded and so far gone that they could not live anyway. It seemed like a brutal thing to turn away and leave a man in a trench to die but circumstances were such at times it was necessary. My impression from the scenes of that day and night was that the whole thing was not worthwhile at the price men were paying in blood and anguish; that if the men at the heads of all the warring governments had to spend a few hours in the hell on earth that was going on around there the war would be over in very short order. I had not then been in the war zone long enough to realize that human life is the cheapest thing in war.

During the cold winter months of 1917-1918 the war in the trenches dragged on. Everyone knew that a big German attack was pending and on March 21, 1918, it began. The Germans launched what was intended to be a conclusive drive to the sea. Gallagher wrote later:

> We were awakened at 4:30 or 5 A.M. by a tremendous din that seemed to shake the earth from its foundation. The crash of guns was so great that it was fused into one tremendous roar.

So began what was to be called "The Second Battle of the Somme." For a week the British fell back, overwhelmed by massive fire power and manpower, staggering with exhaustion and hunger, knowing little of what was happening beyond their own immediate surroundings. On March 28 the remnants of the Gloucesters and their division, the 61st, were ordered to make a stand and launch a counterattack from the village of Marcelcave, 10 miles east of Amiens. They were soon driven back with heavy casualties. In the rout of the preceding days they had lost contact with the ambulance company and had no way to evacuate wounded. Gallagher wrote later:

> Every man who could possibly walk was made to walk off down the road leading to the westward. Many were weak from loss of blood and severe injuries and said they could not walk, but I called their attention to the machine guns of the enemy getting further behind us and told them that before long the place would probably be in enemy hands. I had no idea at the time that this would come to pass so soon but it served to stimulate the men and many who thought they could not walk were able to drag themselves along. A lot of men simply could not walk. For these, we collected from the courtyards all the old French carts, vehicles, and wheelbarrows we could find and loaded up all the wounded we could. Lightly wounded men going back along the road dragged these carts with them. There were still 18 or 20 badly wounded men in the cellars leading off from the courtyard—some of them I had not yet seen and transportation for none of them was available. I was about to descend into a cellar to see the men there who were crying for help when the German shellfire on the village suddenly stopped. The German Very lights began to go up and I saw at once that they had the village cut off. I found that our men had retreated toward the west and had given up the village. Could I get away? Should I run away to save myself and leave the men who were crying to me for help? The decision came fast and easy. I went into the cellar, lit a candle for light, and calmly did what I could for the men.

Now, prisoners of the Germans, Lt. Gallagher and the wounded men spent two nights and two days in that cellar in Marcelcave under shellfire—this time from English guns. Gallagher wrote later:

> Shells crashed into the buildings over our heads and brought down debris into the cellar that nearly buried us. I was almost desperate at the condition of the men, lying there now for their second night with no food, no care, and not much hope of anything better. The men were suffering acutely from their wounds. They were dirty and lousy, of course, including myself.

Determined to get some care for the men, Gallagher managed to climb out of the cellar, was "recaptured" and taken to a German headquarters where he protested to the officers in charge. Some German soldiers were detailed to help get the men out (3 or 4 had already died) and haul them to a dressing station set up under an old factory.

On March 28, 1918, the Official War Diary of the 2/5th Gloucester battalion recorded: "Lt. Gallagher missing." For over three months "missing in action" was the only word his family had of him.

On Easter Sunday, March 31, Gallagher and the other prisoners were moved back and spent several weeks in a German field hospital along the road east of Marcelcave. Gallagher wrote later.

> Conditions here were terrible and not resembling what we usually think of as a hospital. The German advance had been so rapid, with such poor transportation facilities, that little equipment could be carried and nearly everything had to be improvised. No such things as beds; the wounded men were simply packed as close as possible on the bare floor and given very lousy blankets. The cooties seemed to make a racetrack. Medical supplies were lacking, gauze dressing was a rarity. They had a paper substitute—a kind of crepe paper. When it got wet or soaked with blood or pus it immediately went to pieces. When we took these paper bandages off the badly infected wounds the lice swarmed out. Only amputations, drainage, and dressings were done. Anaesthetics were only used in the worst cases and then mostly ethyl chloride. Water was so scarce that none could be used for washing. Men tore and scratched as they lay on the floor until they had no clothes left. Our men received about the same treatment as theirs as far as I could see. There could not be much choice for both received close to the minimum.

In April 1918, with those few English prisoners who could walk, Gallagher was marched further back into German-held territory and was sent to a succession of prison camps, ultimately to a prison camp at Villingen in the Black Forest. Here he joined hundreds of Russian officer prisoners and, to his relief, some other Americans. During the long months behind barbed wire they carved out an existence for themselves based on

Identification picture of Dr. Gallagher on the German prison camp word-of-honor card getting food to eat and trying to read between the lines of the censored German communiques of the war.

When the war was finally over the prisoners of war were eventually released and Gallagher returned to England. On Jan. 30, 1919, he sailed for home, assigned as transport surgeon on the SS "Regina." He reached Waseca on Feb. 26. Of this he wrote later:

> That the joy of being home again compensated entirely for the weeks and months that were gone and soon to be forgotten, I hoped, goes without saying.

But they were not so soon forgotten. These were awkward days for his family. He was depressed and ill at ease. He had a haunted air. After a while he stopped trying to talk about the war and thought about resuming his career.

Starting a surgery fellowship at the Mayo Clinic in Rochester in the spring of 1919, he reentered the world of medicine and surgery which he loved. He also sorted out the diaries, notes, and other items he had brought back from Europe. He no longer spoke of the war. Instead he began to write:

> I write down now, while things are fairly fresh in my memory, some of the events of the past nineteen months which might possibly be of interest to others at some future date when the great World War shall have become a thing of the far distant past. So from memory and from parts of a diary which are at hand I shall attempt to mention at least some of the places I have been and some of the impressions received.

The memories of which he could not speak, the experiences he could not share, the loneliness he could not express he put down on paper, page after page. On June 27, 1920, he wrote: "The story is about done." He finished his account, had a few copies typed for his family, put it away, and never touched it again. There it remained until 1965—a date when World War I had indeed become a "thing of the far distant past."

With plenty of patients and much work under excellent teachers, with long hours on the floors and in the operating rooms, he gradually thawed out. Even a Mayo Clinic Fellow could not work all the time and a young lady who worked at the Clinic attracted his attention. She looked "beautiful, but tubercular," he observed. Beautiful she was, but tubercular no—and on April 12, 1921, he married Margaret Manahan of Chatfield, Minn.

In 1922, restless again, he wanted to get out on his own. He left the Clinic and started practice in his home town, Waseca. He was busy from the start although he did not entirely escape those who remembered "Bennie when he was just a boy." Nor did he escape a kitchen table appendectomy—his first and last. Much later he recalled ruefully that "it was the most normal looking appendix I ever took out!" In 1927 he returned to Rochester for more work in urology, then practiced for a year in St. Cloud with Drs. Freeman and Lewis. In 1929, still restless, he returned to Waseca, this time for good.

With his practice growing Dr. Gallagher worked through the years of the Depression. With his surgical training and the new hospital in town he had much operative work but many deliveries were still done in the home, often far out in the country. Money was scarce in the farm country in the 30s. His charges were as low as he could make them and he seldom sent out bills. He was often paid with poultry, dairy products, and once a whole hog.

He experienced the trials and joys of country practice in Minnesota but it was not practice in isolation. Nearby were the Mayo Clinic where he had trained and to the north the University. He never hesitated to acknowledge what he was not equipped to handle nor to seek expert consultation when necessary. He did not hesitate to give help when it was asked of him. Dr. William C. Bernstein of St. Paul, Minnesota, recalls:

> In 1928 after completing internship I took over a general practice in New Richland, Minn., 12 miles south of Waseca. The memories of my early years of practice are interwoven with the help I received from Dr. Gallagher. He was an outstanding physician and a good friend, kind and compassionate to patients and considerate of a younger colleague.

He had a rare knack for diagnosis, based on careful and exact examination and observation of people. He had little time for those who looked first at lab reports rather than at the patient. Sometimes he seemed almost to fly by the seat of his pants. As a colleague in Rochester put it, "I don't know how he does it out there in the sticks, but if that fellow down the road says a patient has ——, that patient has it!"

Dr. J. L. Tavenner, now of Dixon, Illinois, practiced for five years in Waseca in the 30s. He writes:

> When I started in Waseca thirty-five years ago, it was Ben Gallagher who was friendly and made me feel I would amount to something. He taught me a lot and bailed me out many a time. He represented in medicine the ideals I always felt a good doctor should have. He was conscientious to the extreme and gave of himself when he was overworked and exhausted. He was most capable but always underrated his fine ability.
>
> I remember one thing he told me. "No surgical emergency is so acute as to prevent a doctor from a period of

> careful reflection about the case before final diagnosis and action is made."
>
> I was always so proud that on many occasions Ben used to have me look in on a patient with him and he always made me feel that he really was interested in my opinion. I was the one who gained the most out of the consultation and I have a hunch he just wanted the "young fellow," as he so often called me, to see an interesting case.
>
> Ben was a master of subtle humor and his stories and anecdotes were rare indeed. There was never anything off color either. In fact, I used to tell him he'd never do as a urologist—his vocabulary wasn't raw enough.
>
> I am sure that the best tribute I can say about him is that he just did everyone good who knew him.

Gallagher liked to play golf and shot a creditable game. Although he was a member of Alpha Omega Alpha, honorary medical fraternity, his allegiance belonged to an old high school fraternity known as A.K.T.A. This stood for Alpha Kappa Theta Alpha but the members said it actually stood for "All Kinds of Trash Admitted." Dr. Harold Habein, retired member of the Mayo Clinic staff, who grew up in Waseca, was also a member of the A.K.T.A. and recalls that at their annual reunions "Ben was a mighty sharp poker player. He always had a cigarette in his mouth but he never lit it."

Dr. Habein also recalls a time when Dr. Gallagher had him see a patient in consultation. The patient had right lower quadrant pain and a history of having had his appendix removed three years earlier. A McBurney incision was in clear sight. Dr. Gallagher was sure it was appendicitis in spite of the history; Dr. Habein concurred and sure enough, at surgery they found a red-hot appendix. The patient's family was indignant!

During these years much of his practice was surgical work. Dr. Bernstein writes:

> My association with Dr. Gallagher was between 1928 and 1940. Now that many years have elapsed since I had the privilege of working with him I am in a better position to evaluate the work which he did. He was an excellent surgical technician. He handled tissues gently, prevented excessive blood loss, and was meticulous in his repair of wounds. During the years of his greatest activity Dr. Gallagher performed many major surgical procedures extremely well—leg amputations, caesarean sections, hysterectomies, large and small bowel resections, empyema operations, and many other technical procedures with excellent results without benefit of some of the ancillary services which are available today.

Dr. Gallagher participated actively in the Southern Minnesota Medical Society, presented papers, and was its president in 1936. In his presidential address he discussed what he called his "six beatitudes of conduct in medical practice":

1] Do not discuss your competitors with anybody. We know only too well that the fortunes or misfortunes of medical practice are often regulated by factors over which we have very little control. The streptococcus is deadly, whether in our competitors' practice or in our own.

2] Do not be "uppish" with people who employ another doctor. Against "state medicine" we argue that people must be allowed free choice of physician. We must then allow them that privilege freely ourselves.

3] Do not try too hard to explain reasons for everything, to unscrew the unscrutable, as the Negro preacher expressed it. The art of medicine is based in great part on the skillful use of words, but the science of medicine is seldom if ever improved by verbosity.

4] Make the job the main thing while on it and take vacations away from town.

5] Try to avoid hearing the mean things said about you and if heard, forget them as soon as possible. As the poet expressed, "By thine own soul's law learn to live."

6] Give every case the best attention possible and do not needlessly worry between visits.

He concluded:

> I think another thing which tends to make us unhappy as we grow older is the realization of the fact that we have not accomplished as much in our lives as we had hoped to do. Psychologists tell us that we are born with varying abilities to accomplish. Under our constitution we are said to be created "free and equal" but we know that in any business or profession it is only given to a few to scale the heights of fame and fortune. Perhaps it is just as well that this is so for much of life's work must be done in the valleys and in the lowlands. I do not believe that many wars would ever be won by an army consisting entirely of generals. Not many people in any one community will suffer because of the doctor's inability to diagnose or to cure a brain tumor. A great many more will suffer if the doctors of that community cannot handle their confinement cases intelligently, or cannot diagnose and treat the seven-year itch when they see it.
>
> If we could retain something more of the idea of service with which we entered the study of medicine—the idea that we are trying to do the best we can for people in distress—and if we could induce people to believe that we are doing this, then I think we would come closer to occupying the enviable position in the esteem of the public which the older doctors held. I think that in our concern about the purely economic and scientific features of our profession we are likely to forget that if we are in truth members of the last existing guild we have an obligation to be noble over and above that of the man and woman of almost any other calling.
>
> In dealing with people who cannot well afford to pay much for our services, if we could be willing more often and more graciously to count as part of our compensation the knowledge that we have the power and the privilege "to cure sometimes, to relieve often, and to comfort always" then we would be less inclined to apply the yardstick of monetary income as the main measure of success.

If we are performing a useful work in our community and doing it to the best of our natural born ability, we are achieving success and we should not be too unhappy about it because we are not also acquiring fame.

In common with most people, small frustrations and distractions made him boil, but the more truly serious the situation was the calmer he became. Let a drawer stick and everyone took cover, but a Mexican laborer who appeared at the front door with a knife between his shoulder blades was cared for with aplomb. "All the money in the world would not buy me a pen that will write!" he would explode, but when mayhem actually reigned he was a rock. On country calls he would often take several of his five children for the ride and for their company. Or so it seemed at the time. Actually it provided him with a chance to talk and to listen without interruption. On these rides he loved to tell tales of the early history of the area and along the way imparted much of his own philosophy.

While his approach was usually oblique he went straight to the core of any situation and dispensed with rationalizations in a hurry. "There is no substitute for brains" summed up his view. He seldom advised directly but instead played the devil's advocate. When he did give advice it was usually backhanded. "I'll tell you how I successfully avoided becoming rich."

He had no objection to being a good loser, playing the game for the game, but while you were at it you might as well win. Don't pretend you don't want to win.

He rarely called a child on the carpet directly. He never meted out punishment. He did not need to because the worst punishment was his knowing they had done something wrong. One morning at breakfast he mentioned that he had probably the only car in southern Minnesota, or all of Minnesota for that matter, with grass growing under the right bumper. That was all. He never asked who, how, when, nor mentioned it again, and it never happened again.

Perhaps it is not so much the presence of a father in the home as the reason for his absence that matters. Certainly there was little of the home magazine type of togetherness. He never knew any more about the kitchen than where to find a box of dry cereal and considered eating outside fit only for aborigines. He scarcely knew a hammer from a nail and chose never to learn. The "sick man" came first. This was the norm. He was gone but not because he wanted to be away—it was because someone needed him.

This understanding could come to children only through their mother, and indeed, the day-by-day brunt of family affairs fell on Mrs. Gallagher, who served as filter, buffer, and diplomat.

They were too busy to formulate theories of child raising. Instead, they treated each child as a friend, instilled in them a sense of personal dignity, and reared them in the knowledge that their parents had full confidence in them. This was their discipline.

Sometimes family conversation turned to "the war." Dr. Gallagher's stories were not like the exciting ones to be read in *Sky Fighters* magazine. His had no fierce "Huns" and no bitterness—just discouragement at the pain and folly. No horror for its own sake—just facts related so impersonally that one scarcely sensed he had been part of the events. A friend, a newspaper publisher, read the account he had written and wanted to publish it but he always refused.

In 1939 another war erupted. He identified with his old comrades, the English, during the Battle of Britain, and thought of his old Russian PW friends as Hitler attacked Russia. Now he worked harder than ever. But his perspective didn't change. As part of the Civil Defense program he found time to teach a First Aid course and gave the highest score to a student who answered all questions with "Call a doctor."

In the years immediately following the war he kept on as before. The only way to make him let up was to persuade him to follow his own advice to other doctors "Get out of town." So each year Mrs. Gallagher would develop an uncontrollable yen to see another part of the world, and so get him away. He traveled as he did everything else—from dawn to midnight. He considered himself a man of simple tastes, ready to rough it. Mrs. Gallagher agreed. "Ben's tastes are simple. All he wants is simple luxury!" He believed in maps and compasses, except when they disagreed with his feel of the lay of the land. After ending up in the railroad yards for the third time in a row in one city Mrs. Gallagher said, "I knew it! It's your early environment cropping up!" Ben stomped out of the car, slammed into the back seat and announced, "Since you know so much you drive!"

Signs of fatigue were increasing, and in 1949 came a succession of sleepless nights with obstetric and accident cases, and a heavy daytime operating and office schedule. One night, a long-time patient, a young woman in labor, died suddenly of cardiac arrest. All attempts at resuscitation failed and extraction of the infant revealed a dead baby. Dr. Gallagher was crushed, but he had encountered tragedy before with patients and within his own family and he carried on. This time, though, his grief was profound. He could not seem to pull out of it. A few weeks later he was struck by paralysis of the right side of the body. He could scarcely speak. He had been having nosebleeds and some dizzy spells, but had resisted all attempts of his associate, Dr. Raymond Davis, to examine him.

Ben Gallagher felled by a stroke! It was hard to believe. He returned again to the Mayo Clinic, this time as a patient. The odds said he was finished, that he would never work again. But he had never paid attention to the odds. Never in his life did he put up a braver fight. Gradually some motion came back in his paralyzed right side. He returned home and with the help of his wife, his physicians, and his own grit he progressed. As the months passed he sat up, then stood up, then walked. Eventually he could walk quite well, though with a "snappy" gait. For nine months he spent hours each day exercising his inert right arm on a rotating wheel. By slow degrees it regained strength and agility. He learned to write all over again. Aphasia from the stroke steadily improved. Though his speech never became perfect again it did not interfere with his story-telling ability. Nor was his speech impairment great enough to prevent him from giving his son some salty, astute, and sometimes acid advice about patients.

Dr. Gallagher had always read and been a student of history. Napoleon interested him. He liked Cardinal Newman, read his works, and had been president of the Newman Club while at the University. He loved Abraham Lincoln and read everything he could find about the Great Emancipator. Along with this went his strong interest in the Civil War. He identified with that war more than with the one he had himself experienced. Now he had time to indulge this avocation—for him too much time. As his health improved, he and Mrs. Gallagher visited the old battlefields around Washington and Richmond. They went to Tennessee to the battlefield of Shiloh to look for the grave of a great-uncle he had never known, John Barden.

But the practice of medicine was his prayer. To be shut off from it was to be dead. He returned to practice, although not at the former pace. The birth of their first grandchild in Austria took the Gallaghers to Europe. They toured the continent but Dr. Gallagher chose not to go back to the old landmarks in his life. "They would all look different," was all he said.

When he returned he was restless at being semiretired. To "avoid vacuuming the rugs" he began digging out information on the early medical history of Waseca County. The research revealed some hilarious and skin-blistering feuds between the early doctors. With Dr. J. F. Lynn of Waseca he wrote a series of articles about those days which ran in the June, July, and August 1952 issues of *Minnesota Medicine* as part of that journal's "History of Medicine in Minnesota" series.

He also agreed to serve as city health officer and promptly found himself contending with rats in the dump, algae in the lake, and "mink on the hoof."

In 1956 he was named Waseca County "Father of the Year" in these words:

> We think no citizen of Waseca County is loved by more people than Dr. Ben. His kind and fatherly interest in people goes far beyond his own family and extends to every person who has ever come to him for help.
>
> No one will ever know how much he has done to help people because he is so quiet and unassuming. He is much more than a doctor of physical illness. Many people who are not his patients go to him for encouragement when they are in real trouble. He is truly "father" to the whole community.

On May 28, 1959, the people of Waseca honored him and his brothers, Henry and Frank. Henry, a former chief justice of the Minnesota Supreme Court, and Frank, an associate justice of the court, said that they shuddered when they saw Ben on the witness stand to give medical testimony because they knew they'd get the truth! Each of them claimed to have been the handsomest, smartest, and best ballplayer. In honor of Dr. Gallagher the community made a grant to the Waseca Memorial Hospital and gave him a scroll bearing a citation "in recognition of his outstanding career."

In 1960 Dr. Gallagher began having recurrent bouts of shortness of breath. This he could not fight. "When the ball game is over you leave the field." Flatly and finally he retired. People refused to believe it and continued to seek him out at home. "Doctor Ben knows my case," they said. "Just let me ask him something. It will only take a minute." Despite his growing fatigue he would rally himself and give them the best advice he could; mostly he would tell them to go to the new doctors, the younger doctors. "They know more than us old-timers," he would say with a twinkle.

He was often dyspneic and had lost much weight. He had what he called "a touch" of diabetes which he said he was treating "with contempt" and would heap more whipped cream onto his strawberry shortcake. But his breathing became harder and chest plates showed pulmonary edema. Although his electrocardiograms showed evidence of coronary artery disease he was convinced that his breathing troubles were not primarily due to his heart. It was always regular, his blood pressure was normal, and cardiac medications seemed to scarcely help at all. He was sure he had residual pulmonary fibrosis, a result of gas damage in 1918 when he had been severely gassed twice.

But still he had a quip. Early one morning, rummaging through what he called his drugstore and taking various pills he said wryly, "Think of it. I've already taken eight pills and the day has hardly begun!" He could sleep less and less as the intervals of relief from dyspnea grew shorter. He gave his own prognosis: "Don't worry, I'll beat the clock. The medicine will work longer than I will." When urged to go on anticoagulant medications he said, "No, I'd rather clot to death than bleed to death." Forty years of medical practice had imbued him with a deep-seated skepticism about medicines. "I've seldom been sorry for something I didn't give. But I've often been sorry for something I did give."

In 1920 the young man had written at the end of his account of the war, "The story is about done," not knowing that the real story had only just begun. Now, a grandfather twenty times over, for him the story ended early one October morning in 1962. For four days the people came to say goodbye. They came by the hundreds. They came from miles away, each with a memory to share.

"He saved my daughter's life. Here she is, all grown up."

"He fixed my arm. See it? I thought I was going to lose it."

"He delivered all my babies, all fifteen of them."

"He made me feel better just by coming into the room, even if we both knew there was nothing he could do."

They were speaking of a man who had not been in really active practice for thirteen years and who had been completely retired for two years.

On the fifth day he was buried in the Catholic cemetery on the Minnesota prairie, almost within sight of his birthplace.

Shortly after his death a colleague and patient wrote to Mrs. Gallagher:

> In his passing Dr. Gallagher has left a great void in our community that will not soon be filled. At the same time he has left a great monument of public and personal good for our community and the people in it. Greater even than the relief of our physical suffering was the faith, the hope, and the friendship that he gave us.
>
> Dr. Gallagher was the sort of man we fathers could hope our sons might become, despairing of being his equal ourselves. We know that he gave of his physical strength to the limit, and equally of his limitless spiritual strength. We also know that as his wife you added tremendously to that strength that helped us all so much.
>
> My deepest sympathy goes out to you in your bereavement, and yet I envy you your years of being close to one who I have long felt to be an ideal of professional acumen, human understanding, and personal charm.
>
> May Dr. Ben rest in peace.
>
> (signed)
> Leland West, D.V.M.
> Waseca, Minn.

NEONATAL THYMECTOMY produces runting in mice. Injection of adult spleen cells from a donor with identical genetic makeup (syngeneic) restores normal body growth. Injection of adult syngeneic thymocytes reverses wasting in only a few, however. Allogenic adult spleen cells fail to alter wasting, probably as a consequence of homologous disease produced by injection of immunologically active cells capable of rejecting host tissue. The essential element in reversal of this wasting may be the increased immunologic capacity conferred by injections of immunologically competent spleen or thymic cells. Spleen cells from animals that have been cured of wasting have greater immunologic reactivity than those from untreated thymectomized mice.

HENRY R. HILGARD, M.D., EDMOND J. YUNIS, M.D., KENNETH SJODIN, CARLOS MARTINEZ, M.D., and ROBERT A. GOOD, M.D., University of Minnesota, Minneapolis. Reversal of wasting in thymectomized mice by the injection of syngeneic spleen or thymus cell suspensions. Nature (Lond.) 202:668-670, 1964.

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Occasionally, therapeutic failure is due to the patient's inability to mobilize his defenses sufficiently to overcome infection. Typical of this is the debilitated patient, the premature infant, or the diabetic. It is in these patients that the high levels of antimicrobial activity of Ilosone are especially useful. Ilosone has demonstrated antibacterial levels two to four times those of erythromycin base or stearate. Furthermore, it attains them earlier and maintains them longer. Even the presence of food does not appear to affect the activity of Ilosone.

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Dosage: *Children under 25 pounds*—5 mg. per pound of body weight every six hours. *Children 25 to 50 pounds*—125 mg. every six hours. *Adults and children over 50 pounds*—250 mg. every six hours. For severe infections, these dosages may be doubled.

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Book Reviews . . .

Hypertensive Retinal Disease

by SAMUEL A. SHELBURNE, M.D., *48 pp., ill., Grune & Stratton, New York City, 1965. $7.75*

S. A. Shelburne's forty-eight page book deals with a few specific aspects of hypertensive retinal disease rather than covering the entire subject. The first chapter reviews his interest in the hypertensive field; the second, his technique for ophthalmoscopic examination and his reasons for avoiding a numerical grading system to classify the retinopathy. Two chapters describe the appearance and significance of arteriovenous nicking and segmental arteriolar narrowing, findings most important to the author in evaluation of hypertensive retinopathy. A chapter relates hypertension to arterial and venous thrombosis, serous retinal detachment, and microaneurysms. These associations are confusing and questionable. The final chapters discuss papilledema and the use of terms "copper wire, silver wire, and sheathing."

Hypertensive retinal disease is an excellent subject for a current book. This book, however, is disappointing. It is poorly organized, poorly illustrated, and contains inaccurate information. The bibliography is incomplete and out-of-date. The author fails to include the good, current, accepted ideas of many men in the field. The useful information has been previously published in three journal articles by the author.

This book adds nothing more.

B. J. POLEY, M.D.
Minneapolis

Pharmacology and Therapeutics

by ARTHUR GROLLMAN, *6th ed., 1181 pp., ill., Lea & Febiger, Philadelphia, 1965. $15*

This is an authoritative text in pharmacology. The general action of all medications and their basic mechanisms are first described. The anesthetic agents are discussed in regard to their advantages and disadvantages and the different stages of anesthesia. The chemistry, toxicity, mechanism of action of the barbiturates, and opium alkaloids are very adequately covered.

The author develops each subject with its chemistry, site of action, toxicity, and therapeutic uses. The text is written in such a manner as to make the material stimulating to read with its practical application. This book is of great value to all physicians, and it is a must for all interests.

DONALD S. AMATUZIO, M.D.
Minneapolis

Comparative Biochemistry of Arginine and Derivatives

Edited by G. E. W. WOLSTENHOLME, F.R.C.P., *and* MARGARET P. CAMERON, M.S., *103 pp., ill., Little, Brown and Co., Boston, 1965. $2.95*

This little volume is the report of the Ciba Foundation Study Group No. 19 held in honor of Professor J. Roche. There are four papers: "New Aspects of the Metabolism of Arginine," by N. van Thoai; "Homoargine, γ-Hydroxy-

(Continued on page 18A)

DEPROL®

meprobamate 400 mg. +
benactyzine hydrochloride 1 mg.

Indications: 'Deprol' is useful in the management of depression, both acute (reactive) and chronic. It is particularly useful in the less severe depressions and where the depression is accompanied by anxiety, insomnia, agitation, or rumination. It is also useful for management of depression and associated anxiety accompanying or related to organic illnesses.

Contraindications: Benactyzine hydrochloride is contraindicated in glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

Precautions: *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of preexisting symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

Benactyzine hydrochloride—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

Meprobamate—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Dosage: Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

Supplied: Light-pink, scored tablets, each containing meprobamate 400 mg. and benactyzine hydrochloride 1 mg.

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(Continued from page 16A)

arginine, and Related Compounds," by E. A. Bell; "Transamidination and the Biogenesis of Guanidine Derivatives," by J. B. Walker; and "Co-ordination Between Repression and Retroinhibition in Control of a Biosynthetic Pathway," by L. Gorini and E. B. Horowitz. The discussion following each paper and the general discussion at the end of the session, as is customary in these reports, are given in full. They are thought-provoking and raise more questions than are answered.

Arginine has long been known as a substance of exceptional interest but its biological role apparently is more important than was originally expected. These papers give a comprehensive summary of past knowledge regarding the biochemistry of arginine and present a wealth of new material, clarifying, in particular, various aspects of the biochemictry of guanidine derivatives.

The book will be of great value to biochemists, physiologists, and microbiologists. The use of enzyme content for the taxonomy of the Papilionoideae will fascinate botanists and undoubtedly lead to further collaboration with biochemists. For the busy physician, however, the book will be of but passing interest.

DAVID B. SABINE
Yonkers, N.Y.

Uterosalpingography in Gynecology: Its Application in Physiological and Pathological Conditions

by SAMUEL ROZIN, M.D., *366 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $20.50*

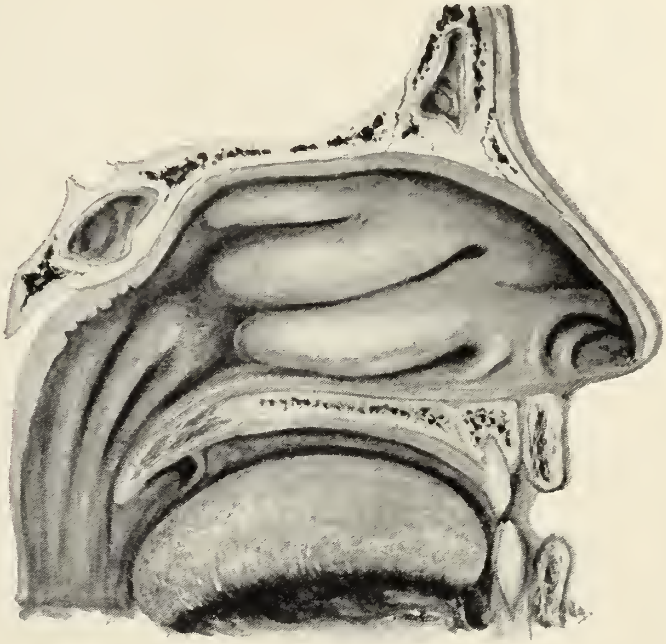
Seldom in medicine are the contents of a book devoted to a single diagnostic procedure, but such is the case with uterosalpingography in gynecology. As might be expected, it is composed largely of reproductions of uterosalpingographic films. However, a rather complete text accompanies this material.

The book is divided into eight parts covering general principles of uterosalpingography; uterine and tubal function; developmental anomalies of, and pathological changes in the uterus and tubes; recurrent abortion, including cervicography, and dysmenorrhea; genital tuberculosis and fistulae; pathology of the fallopian tubes, pelvic peritoneum, and ovary; and a miscellaneous part devoted to uterography in early pregnancy, intrauterine pessary, and accidental intravasation of contrast medium. Every part contains from two to four chapters, each with a bibliography. As might be expected, the entire bibliography of the book becomes extensive.

Along with a narration of the development of uterosalpingography, the author discusses the merits of the various contrast media and then describes his own modifications of the technique. The technique of television fluoroscopy could have been described in more detail as it is one which has not been widely exploited nor will it be readily available to many readers.

The book is replete with well-chosen photographs of uterotubal and pelvic radiographs as seen in various developmental and pathological conditions. Each and every set of radiographs is accompanied with an adequate text. This volume should be of definite value as an aid to clearing up obscure diagnosis in certain gynecic problems.

CLAUDE J. EHRENBERG, M.D.
Minneapolis



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Hydrochloride ....1.25 mg.
'Sudafed'® brand Pseudoephedrine
Hydrochloride ....30 mg.
Bottles of 1 pint.

Dosage and Administration	**Tablets**	**Syrup**
Adults and children over 6 years of age	1	2 tsp.
Children 4 months to 6 years of age	½	1 tsp.
Infants up to 4 months of age	—	½ tsp.

Dosage indicated may be given 3 times daily.

Side effects: While the great majority of patients will experience no side effects on 'Actifed' therapy, those sensitive to the component drugs may exhibit mild stimulation or mild sedation. No serious side effects have been noted.

Caution: Although pseudoephedrine hydrochloride is virtually without pressor effect in normotensive patients, it should be used with caution in patients with hypertension. In addition, even though triprolidine hydrochloride has a low incidence of drowsiness, appropriate precautions should be observed.

Complete literature available on request from Professional Services Dept. PML.

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News Briefs . . .

North Dakota

DR. C. B. HIGGIE of London, England, has opened practice in the Nelson County Memorial Hospital in Michigan, N.D.

* * * *

DR. DONALD E. LORENTZEN has joined the staff of the Hettinger Clinic. Dr. Lorentzen received his medical degree in 1961 from Northwestern University, Chicago, and is a member of the American Academy of General Practice.

* * * *

DR. LEONARD W. LARSON, Bismarck, has been elected president of the American Cancer Society. He is a former president of the American Medical Association. Dr. Larson has been a director of the Society since 1941.

Minnesota

DR. THADDEUS J. LELWICA of Staples has been elected to the American Academy of General Practice.

* * * *

DR. L. ASHLEY WHITESELL, Shakopee general practitioner, has joined the Buffalo Clinic.

* * * *

DR. F. EDMUND DONOGHUE, Mayo Clinic specialist in chest diseases, has been elected president of the Zumbro Valley Medical Society. Also elected were two Rochester physicians, Dr. Malcolm K. Campbell, vice-president, and Dr. David C. Utz, secertary-treasurer.

* * * *

DR. ROGER P. HALLIN of Minnetonka has been named director of rehabilitation services at the Kenny Rehabilitation Institute, Minneapolis. He replaces Dr. Herbert A. Schoening, who has become director of the department of physical medicine and rehabilitation at St. Mary's Hospital, Minneapolis.

* * * *

DR. BERNARD H. HANSON, originally of Moorhead, is now practicing at the Northern Itasca Hospital, Bigfork.

* * * *

DR. DONALD R. MUELLER has joined the staff of the Itasca Memorial Hospital, Grand Rapids, as a radiologist. Dr. Mueller will provide diagnostic services not only at Itasca Memorial Hospital but also at hospitals in Deer River and International Falls. He will commute to International Falls by airplane.

* * * *

DR. SALVATORE VERTUCA has been appointed head of the five-county mental health center at New Ulm.

* * * *

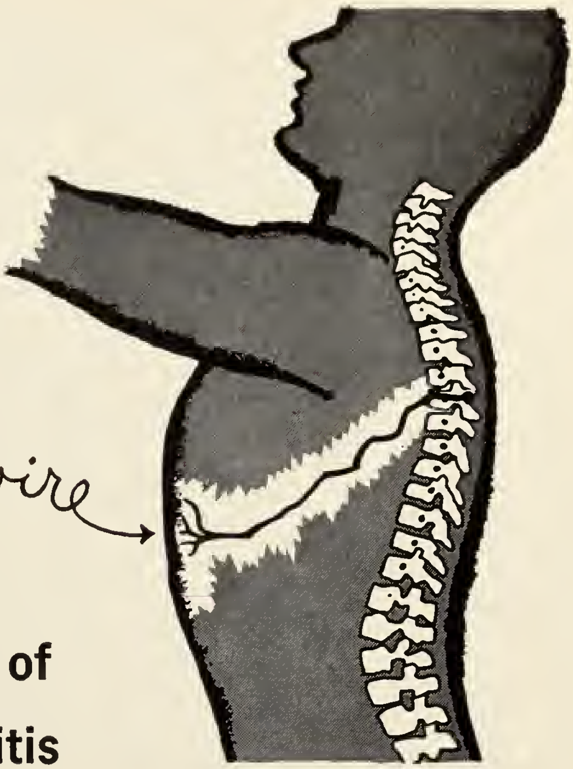
DR. ALBERT E. MEINERT, a Winona clinic staff physician for the past thirty-eight years, has retired. Dr. Meinert will spend his winters in San Diego, Calif., and summers at his lake home near Hayward, Wis.

* * * *

DR. DONALD E. STEWART, Crookston physician, has been elected president of the Minnesota Division of the American Cancer Society, succeeding Dr. Philip F. Eckman, Duluth.

(Continued on page 22A)

Like a Red Hot wire



the Searing *Pain* of Inflammatory Neuritis

PROTAMIDE®

colloidal solution
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proteolytic enzyme

provides the *selective* fast-acting relief . . .

Repeatedly in published clinical studies,[1-10] investigators stress the following therapeutic characteristics:

- relief of inflammatory pain (non-traumatic) is prompt—particularly when administered early.[1-4]
- disability time is shortened from weeks to days.[7]
- so specifically effective is Protamide that a positive response is diagnostic of inflammatory neuritis.[3,4]
- prompt relief is observed even in ophthalmic herpes zoster.[5,6]
- incidence of sequelae such as postherpetic neuralgia is reduced.[1-4]
- consistently described as the therapy of choice.[1,3-6]

Administration:
In neuritis and herpes zoster, one ampul I.M. daily for 2 to 5 days usually relieves pain completely in patients treated early. Well tolerated.[1-10] However, inadvertent intravenous administration may cause anaphylactoid reaction.

—Boxes of 10 ampuls, 1.3 cc. each.—

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NEWS BRIEFS

(Continued from page 20A)

THIRTEEN MINNESOTA SURGEONS have been inducted by the American College of Surgeons. Included are Drs. Yrjo K. Gronquist, Cloquet; John B. Sanford, Duluth; Donald C. Meredith, Mankato; George O. Hilgermann, Michael F. Lynch, John C. Parrott, Jim L. Story, and John F. Waldron, all of Minneapolis; D. Thane Cody, Clyde Culp, Eric Lofgren and Donald McIlrath, all of Rochester, and Thomas Murphy, Stillwater.

* * * *

DRS. A. J. LEHRER and BEN M. TUMA, both of Montgomery, have closed their Family Medical Clinic offices in Waseca and will now practice only in Montgomery.

* * * *

DR. DALLAS D. GLICK has resumed his practice in Mountain Lake in association with Dr. Alvin Wiens in the Manor Medical Building. Dr. Glick recently received his master's degree in surgery from the University of Minnesota Graduate School of Medicine at Rochester and has been certified by the American Board of Surgery.

* * * *

DR. FRANCIS R. KEATING, Mayo Clinic physician, has been appointed to a three-man panel of experts on thyroid gland disease. The panel will try to determine whether a link exists between nuclear fallout and thyroid disorders in young people near above-ground atomic bomb test sites. The panel, appointed by U.S. Surgeon General William H. Stewart, will investigate 70 affected young persons at St. George, Utah, and 25 affected youngsters at Safford, Ariz. St. George has experienced the nation's highest exposure to radiation from the Nevada atmospheric tests, whereas exposure in Safford has been about average for the nation.

* * * *

DR. LLOYD E. HARRIS, consultant in pediatrics at the Mayo Clinic, has been elected a member of the American Board of Pediatrics. His term will expire in six years.

* * * *

DR. SHELDON L. MANDEL of Minneapolis has been elected president of the Minnesota Dermatological Society.

* * * *

DR. WESLEY W. SPINK, University of Minnesota professor of medicine, recently served as the first visiting professor of medicine at the University of Arkansas Medical School, Little Rock. During November, Dr. Spink presented two formal lectures there on his research in brucellosis and shock and conducted clinics and informal conferences.

* * * *

THE MAYO CLINIC PROGRAM of clinical reviews of general problems in medicine and surgery will be held in identical sessions March 28 through 30 and April 4 through 6, 1966. This program is acceptable for credit by the American Academy of General Practice and the College of General Practice of Canada. Registration is $10. Those wishing to attend should communicate with M. G. Brataas, Mayo Clinic, Rochester, indicating which session they prefer to attend.

South Dakota

DR. ROBERT H. HAYES, Winner physician and surgeon, has left his practice for twelve to fourteen months to become a member of a surgical team in South Viet Nam. Dr.

(Continued on page 24A)

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FROM
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The Most Dependable Leasing Service Available to the Medical Profession

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(Paracotes*)

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*PARACOTES—Trademark for specially manufactured TIMED DISINTEGRATION CAPSULES

Of 80 mg. PETN DOSAGE . . .

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"In general a ('Paracote'-TDC-Capsule) has one feature that no timed-disintegration tablet can have. If the dosage in tablet form is taken during or close to mealtime it may become embedded in a food mass. Until the digestive process liquefies that food mass and frees the tablet, the release process is totally arrested. It is inconceivable that any more than a very small percentage of the hundreds of pellets from one of our ('Paracotes'-TDC-Capsules) could be so impeded. Our preference for the 'Paracotes' form of capsule is no mere bias."

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(Continued from page 22A)

Robert Stiehl of Burke has assumed Dr. Hayes' practice for the interval.

Deaths . . .

DR. FREDRIK I. LOTTSFELDT, 30, former head of the children's division of leukemia research at University of Minnesota Hospitals, died Nov. 12 following a car accident in Washington, D.C. A fund in Dr. Lottsfeldt's honor is being established at the National Cancer Institute in Washington. Contributions may be sent to Dr. Seymour Perry at the Institute or Dr. William Krivit, department of pediatrics, University of Minnesota Hospitals.

* * * *

DR. ROSCOE C. HUNT, 82, life-long Fairmont, Minn., physician who has been in retirement for several years, died Nov. 12 at a nursing home in Rhinelander, Wis. Dr. Hunt received his medical degree in 1909 from Harvard Medical School and was a member of the American College of Surgeons.

* * * *

DR. LEONARD T. CARLSON, 61, a staff member at North Memorial and Glenwood Hills hospitals, Minneapolis, died Oct. 19. Dr. Carlson had practiced medicine in North Minneapolis for thirty-four years and was a medical examiner for the selective service board since 1941. He received his medical degree in 1931 from the University of Minnesota and was a member of the American Academy of General Practice.

* * * *

DR. LUCIUS H. FOWLER, 69, a fellow in surgery at the Mayo Graduate School of Medicine from 1921 to 1924, died at his home in Newport Beach, Calif., Oct. 13. Dr. Fowler graduated from the University of Minnesota Medical School in 1921 and received his master of science degree in surgery from the same school in 1925. He was a fellow of the American College of Surgeons.

* * * *

DR. JOHN R. MINER, 73, retired Mayo Clinic staff member, died Nov. 2 in Rochester. Dr. Miner received his doctor of science degree in biometry and medical statistics from Johns Hopkins University School of Hygiene and Public Health in 1922. He was the author of more than sixty papers, and he was a member of the section of publications at the Mayo Clinic from 1938 until he retired in 1957.

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Contraindicated in comatose or greatly depressed states due to CNS depressants and in cases of existing blood dyscrasias, bone marrow depression and pre-existing liver damage. *Principal side effects,* usually dose-related, may include mild skin reaction, dry mouth, insomnia, fatigue, drowsiness, dizziness and neuromuscular (extrapyramidal) reactions. Muscular weakness, anorexia, rash, lactation and blurred vision may also be observed. Blood dyscrasias and jaundice have been extremely rare. Use with caution in patients with impaired cardiovascular systems.

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Pediacof®

Each teaspoon (5 ml.) contains codeine phosphate 5 mg., Neo-Synephrine® hydrochloride (brand of phenylephrine hydrochloride) 2.5 mg., chlorpheniramine maleate 0.75 mg. and potassium iodide 75 mg.

soothing decongestant and expectorant

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nasal drip
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running nose
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eases expectoration

bright red, pleasant-tasting, raspberry-flavored syrup

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Dosage: Children from 6 months to 1 year, ¼ teaspoon; from 1 to 3 years, ½ to 1 teaspoon; from 3 to 6 years, 1 to 2 teaspoons; and from 6 to 12 years, 2 teaspoons. These doses are to be given every four to six hours as needed.

How supplied: Bottles of 16 fl. oz.

Available on prescription only.
Exempt Narcotic.

Side effects: The only significant untoward effects that have occurred are mild anorexia and an occasional tendency to constipation. However, discontinuance of Pediacof has seldom been required. Mild drowsiness occurs in some patients but, when cough is relieved, the quieting effect of Pediacof is considered beneficial in many instances.

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Caution should be exercised if Pediacof is administered to patients with cardiac disorders, hypertension or hyperthyroidism.

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FEBRUARY 1966

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Papaverine hydrochloride	16 mg.
Aluminum aspirin	300 mg.
Phenylephrine hydrochloride	5 mg.
Chlorpheniramine maleate	2 mg.
Vitamin C	100 mg.

Dosage: Adults, 1 capsule 3 or 4 times daily; children, according to age and weight.

Indications: Cough, congestion, headache, discomfort and muscular aches and pains in coryza, rhinitis, sinusitis, pharyngitis, laryngitis, tracheitis, bronchitis, grippe, influenza and pneumonia.

Side effects and precautions: Side effects are infrequently encountered. Codeine and aluminum aspirin should not be given to patients with known idiosyncrasies to these drugs. Antihistaminic agents may cause drowsiness in susceptible individuals. Colrex Compound should be used with caution in hypertensive patients.

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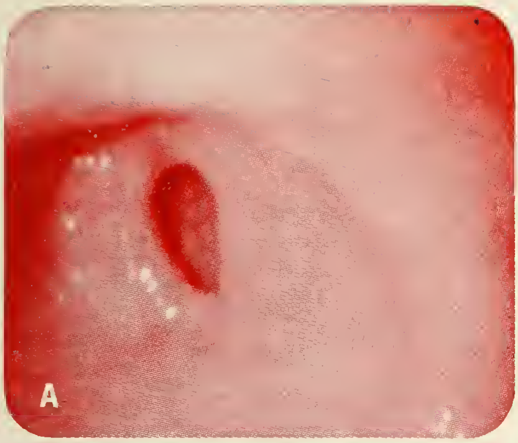
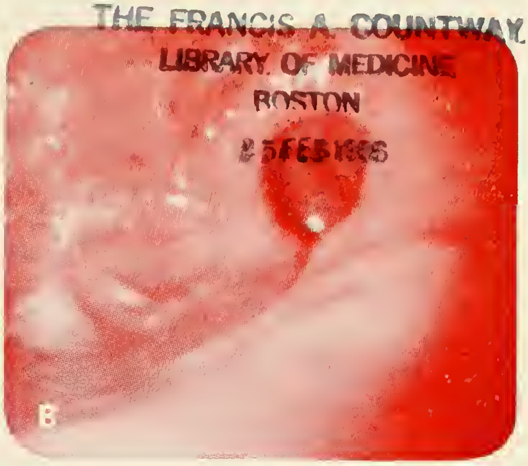


Which Is Pyloroplasty with Vagotomy?



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The Journal-Lancet

Volume 86, No. 2, FEBRUARY 1966

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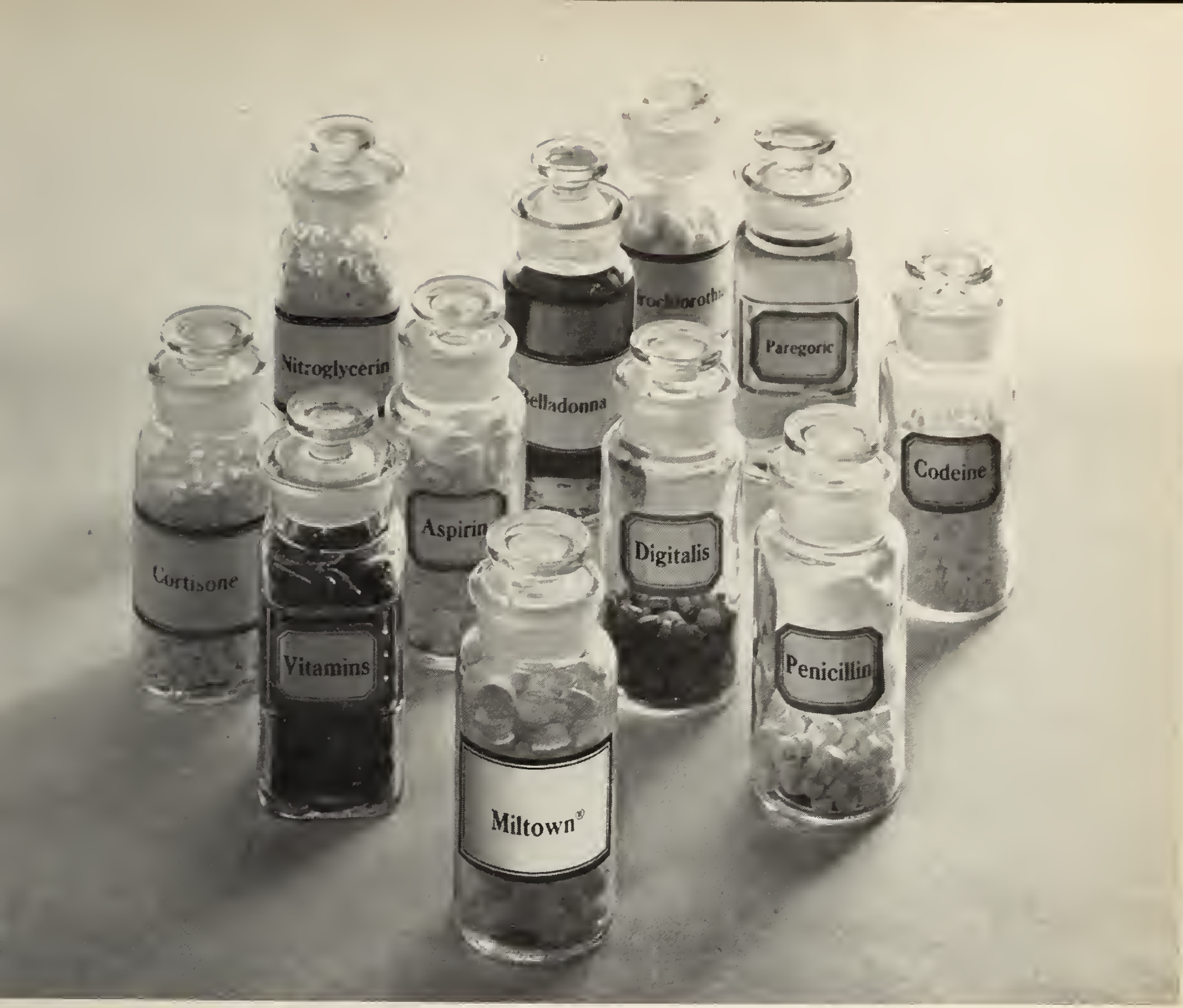

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Precautions: Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of preexisting symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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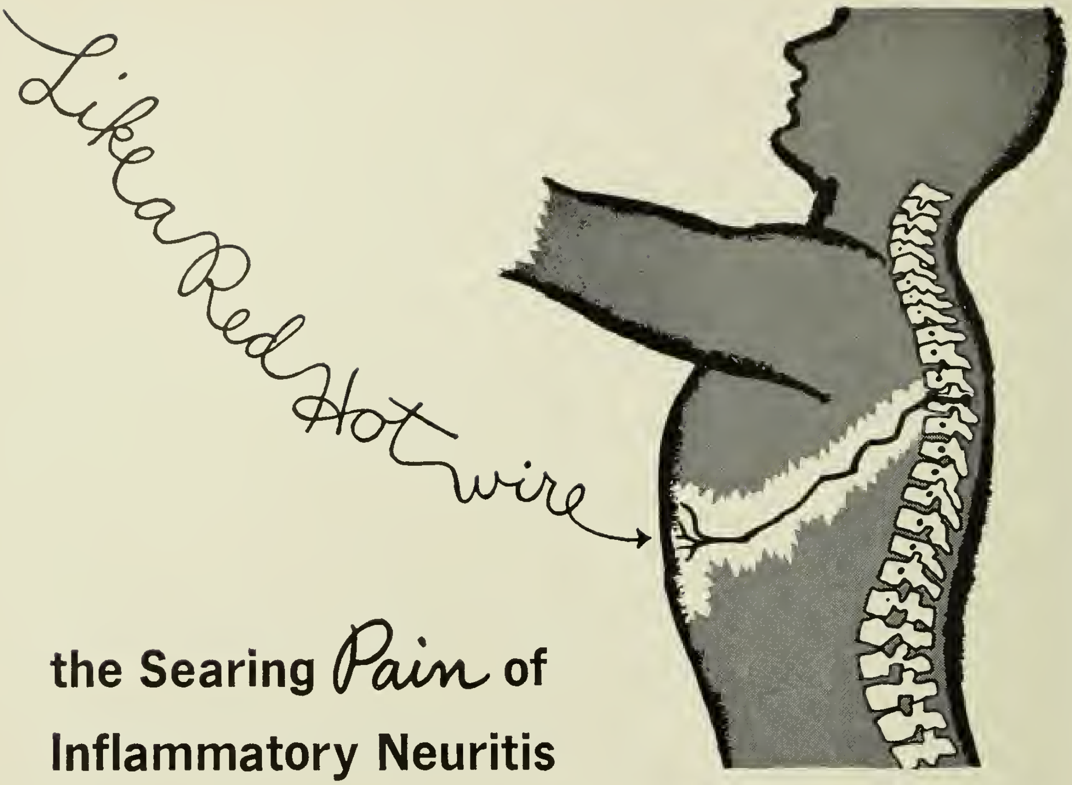
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PROTAMIDE® colloidal solution of denatured proteolytic enzyme

provides the *selective* fast-acting relief . . .

Repeatedly in published clinical studies,[1-10] investigators stress the following therapeutic characteristics:

- relief of inflammatory pain (non-traumatic) is prompt—particularly when administered early.[1-4]
- disability time is shortened from weeks to days.[7]
- so specifically effective is Protamide that a positive response is diagnostic of inflammatory neuritis.[3,4]
- prompt relief is observed even in ophthalmic herpes zoster.[5,6]
- incidence of sequelae such as postherpetic neuralgia is reduced.[1-4]
- consistently described as the therapy of choice.[1,3-6]

Administration:
In neuritis and herpes zoster, one ampul I.M. daily for 2 to 5 days usually relieves pain completely in patients treated early. Well tolerated.[1-10] However, inadvertent intravenous administration may cause anaphylactoid reaction.

—Boxes of 10 ampuls, 1.3 cc. each.—

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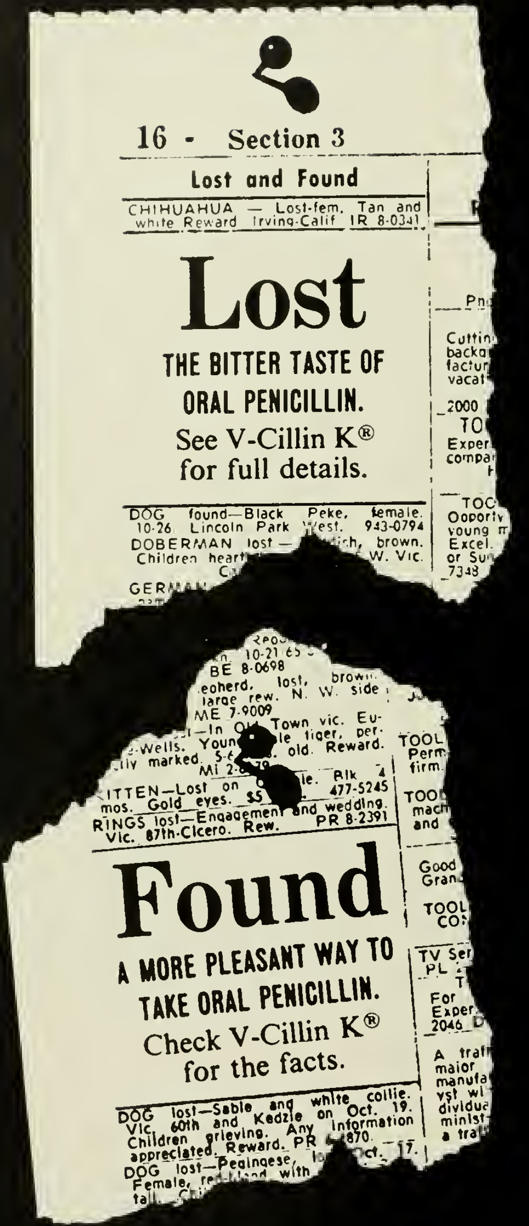

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Some Problems in the Management of Congestive Heart Failure

RALPH R. REED, M.D., and MILTON W. ANDERSON, M.D.
Rochester, Minnesota

IN THE MANAGEMENT of the congestive heart failure symptom complex it is exceedingly important to understand that this syndrome is a gross clinical manifestation which various etiologic processes may share in common. To approach the patient who manifests the congestive syndrome with a therapeutic program of digitalis, diuretics, and salt-poor diet without understanding his disease is contrary to good clinical practice and may possibly be an injustice to the patient.

It is perhaps patronizing to remind practitioners that arteriosclerosis, rheumatic fever sequelae, hypertension, syphilis, and congenital defects are the commonest causes of congestive heart failure, but it is probably less well known that each can produce a similar picture when heart failure develops. These etiologic factors, in common with the more obscure causes of congestive failure, may be influenced by complicating factors that obscure a straightforward understanding of the altered physiologic state.

While emphasizing that a clear understanding of this altered physiology in the patient with heart failure is of great importance, we must also be realistic enough to realize that all the facilities for complete cardiodynamic investigation are not available to the majority of practitioners. Fortunately, such a complete investigative appraisal is usually unnecessary. It is not economically feasible, or humane, to subject each patient to full-scale or complete cardiovascular investigation.

With the usual patient we can rely on a thorough history and physical examination, together with experience-tempered judgment, for satisfactory clinical management. In all situations, however, we must remain alert for the unusual, constantly being aware of the clues which usher in various confusing and complicating factors that influence satisfactory results.

We must understand that the so-called refractory state may have multifaceted causes. The following outline, by Spiotta,[1] points up many of the factors and influences which may contribute to the apparently refractory state in congestive heart failure. Many of these factors may be altered enough to change a picture from one of intractability to satisfactory management.

FACTORS PRODUCING RESISTANT HEART FAILURE

I. *Cardiac*
    A. Active carditis
    B. Silent or masked myocardial infarction
    C. Arrhythmia
    D. Constrictive or effusive pericarditis
    E. Obscure heart disease
        1. Fibroelastosis
        2. Collagen disorder
        3. Amyloidosis
        4. Neoplasm
        5. Polycythemia and so forth

RALPH R. REED *is a fellow in medicine, Mayo Graduate School of Medicine (University of Minnesota), and* MILTON W. ANDERSON *is with the Section of Medicine, Mayo Clinic, Rochester, Minnesota.*

- II. *Extracardiac*
  - A. Renal failure
  - B. Hepatic failure
  - C. Hypermetabolic states
    - 1. Infectious diseases
    - 2. Anemia
    - 3. Thyrotoxicosis, Cushing's syndrome
    - 4. Avitaminosis, especially thiamine
  - D. Atrioventricular communications and Paget's disease
  - E. Pulmonary disease with pulmonary hypertension
- III. *Therapeutic*
  - A. Nutritional
    - 1. Excess sodium
    - 2. Excess calories
    - 3. Electrolyte imbalance
    - 4. Excess water
  - B. Digitalis
    - 1. Excess or deficiency of digitalis
      - a. Potassium excess or deficiency
  - C. Diuretic refractoriness
    - 1. Hypochloremic alkalosis ± hypokalemia
    - 2. Hyponatremic dilutional syndrome
    - 3. Low-salt syndrome
    - 4. "Tight leg" and "tight abdominal ascites" syndromes
    - 5. Hyperaldosteronism
    - 6. Hypoproteinemia
    - 7. Drug antidiuretic influences

We have elected to consider in more detail a few problems in the management of congestive failure under the following headings: [1] diagnosis of cardiac defect, [2] influences of digitalis, [3] effects of arrhythmia, [4] hyperthyroidism, [5] renal and electrolyte problems, [6] thromboembolism in heart failure, and [7] pregnancy and heart disease.

DIAGNOSIS OF CARDIAC DEFECT

Recognition of the specific anatomic defect is a most important aspect of this entire problem. Occasionally, of course, the specific anatomic diagnosis will remain a confusing and unsolved problem, but often the recognition of the defect will permit specific therapy. This recognition is especially timely in this era when surgical treatment for mechanical defects can evoke cures or gratifying palliation.

Active carditis, infectious disease, hemochromatosis, cardiac neoplasms, systemic hypertension, and endocrinologic hypofunction and hyperfunction are examples of etiologic factors which may produce congestive failure and which are amenable to specific therapy capable of relieving or palliating the syndrome. Awareness of these various causes, after a careful clinical examination, may supply the appropriate diagnosis. At times, more extensive laboratory procedures, or even hemodynamic measurements and angiographic techniques, will be necessary for the establishment of a diagnosis. Rarely, even surgical exploration can be justified when there is a strong clinical suspicion of pericardial effusion or pericardial constriction.

The practitioner must weigh the relative values of these procedures, taking into account many imponderables in the patient's entire clinical picture. The greatest potentiality of the art of medicine is realized in these situations, and the experienced physician may have considerable advantage in making this judgment. A lack of experience in cardiology is an indication to refer the puzzling patient for specialty consultation and study.

The array of therapeutic tools at the disposal of the physician may be a temptation to defer the difficult problem of specific diagnosis and await the results of a therapeutic test. It should be emphasized that this type of delay may seriously jeopardize the patient's chance for help by allowing him to fall insidiously into an intractable and irreversible state. Understanding the morbid anatomy and physiology, therefore, continues to be most important for the insurance of proper and timely therapy.

INFLUENCES OF DIGITALIS

William Withering anticipated by nearly two hundred years our continued fascination and utilization of digitalis as a valuable drug, and he also made observations of possible toxic effects which are still valid. Monographs and research papers that attempt to summarize and explain the use of digitalis appear regularly in the medical literature. Proper dosage of one of the digitalis preparations continues to be a mainstay for bolstering function of the failing myocardium.

We want to consider some of the toxic attributes of this drug which can worsen the clinical state. Classically, green and yellow vision, dizziness, syncope, paresthesias, psychosis, and gastrointestinal complaints are symptoms each physician anticipates with overdosage of digitalis. Newer preparations that are more completely absorbed and have a more rapid onset of action than older preparations have robbed the physician of many of these traditional warnings. The therapeutic dose is thought to be about 60% of the toxic dose, and accumulation is a property of most digitalis preparations.[2] Clinical observations suggest that the therapeutic level approaches the toxic level when heart failure worsens with associated increasing cardiomegaly. Consequently, it is possible to miss a narrow therapeutic range in the severely ill patient unless great care is used when titrating the digitalis dosage for each patient individually.

The toxic effects of digitalis may have both a direct and an indirect deleterious influence on the decompensated cardiac patient. Through the production of abnormal rhythm mechanisms, the cardiac output may fall. Depressive states and malnutrition, with their harmful effects on the well-being of the patient, can also ensue from the central nervous system and the gastrointestinal toxicity of digitalis. Almost any cardiac arrhythmia may be associated with digitalis toxicity. Multiple premature contractions, bigeminal rhythms, and persistent regular tachycardia representing a 2-to-1 atrioventricular block and also various degrees of atrioventricular block are all examples of such disturbances that may reduce effective cardiac output.

Considerable attention has recently been given to paroxysmal atrial tachycardia with block as an accompaniment of digitalis toxicity. It may be possible to differentiate this digitalis-induced arrhythmia from a similar, though uncommon, intrinsic arrhythmia not associated with digitalis usage by electrocardiographic, therapeutic, or carotid sinus maneuvers.[3] The presence of this interesting arrhythmia which is recognized only by electrocardiographic study, however, should always alert the practitioner to possible digitalis toxicity. Therapy for this arrhythmia, when digitalis has been administered to the patient, always entails withdrawal of the drug. Cautious administration of potassium ion is advisable, and frequently results are dramatic. The use of cardiac depressants such as procainamide may be justified in some cases.

One must keep in mind that the arrhythmias associated with digitalis toxicity are not always related to the size of the dose but that wide individual tolerance exists. It is also worth emphasizing that arrhythmias which are a toxic manifestation of digitalis ingestion may contribute to refractory congestive failure and that the refractory state may respond to digitalis withdrawal by enhancing cardiac output. The mechanism of arrhythmia and digitalis intoxication appears to correlate with its inotropic effect on the myocardial cell membrane, in which it influences transmembrane movement of potassium ion. Hypokalemia produced by diuretic drugs or gastrointestinal malfunction makes the myocardium more susceptible to the arrhythmic influence of digitalis.[2]

EFFECTS OF ARRHYTHMIA

We have indicated in the preceding paragraphs that arrhythmias related to digitalis therapy may be a factor in the causation of a refractory state of congestive failure. Similarly, other cardiac arrhythmias which are too rapid or too slow or which reduce cardiac efficiency by producing a variable rate will compromise ventricular filling and seriously impair myocardial hemodynamic function. Such arrhythmias, which may be tolerated by the healthy heart, may thrust the patient whose heart is afflicted with disease into a serious or even intractable state of congestive failure. Recognition of the arrhythmia and its etiologic factors are important in their relation to the management of congestive heart failure. In the diseased heart almost any arrhythmia may initiate or prolong failure.

Atrial fibrillation is probably the commonest arrhythmia associated with heart failure. Conversion of this arrhythmia to a normal rhythm or, at least, control of the rate may contribute greatly to satisfactory management of the patient. Pharmacologic conversion of atrial fibrillation with quinidine is less effective and perhaps has greater risk when high doses are needed than has electroversion, as described by Lown and associates.[4] Generally, in the presence of great cardiomegaly or uncorrected valvular defects, atrial fibrillation recurs with such frequency that controlling the rate with digitalis is preferable to repetitive attempts to convert the arrhythmia, either pharmacologically or electrically. Electroversion is the treatment of choice for the management of patients with atrial flutter and with ventricular tachycardia.

Atrioventricular block, especially when it is of minor degree in which an effective cardiac rate is maintained, may be ignored electively. When serious bradycardia occurs, however, which is associated with congestive heart failure, angina, or syncope, treatment becomes imperative. Digitalis must be used with caution in such situations, and the use of cardiac accelerator drugs such as ephedrine and isoproterenol (Isuprel®) is often disappointing. Isuprel® is most valuable when used intravenously by a slow dilute infusion for the patient who has total heart block and repeated Adams-Stokes attacks. In this situation it may be a most effective emergency measure. Heart block causing severe bradycardia, even though stable and not producing syncope, may reduce cardiac output sufficiently to result in refractory congestive heart failure. Experience in a limited number of such cases has demonstrated the value of implantation of an electric pacemaker which, by increasing cardiac rate, ensures an adequate cardiac output to permit diuresis and satisfactory control.

HYPERTHYROIDISM

Masked hyperthyroidism and its relationship to congestive heart failure presents an infrequent but nevertheless significant problem in the management of any large group of patients who have congestive heart failure. Ordinarily, hyperthyroidism is not difficult to diagnose in the young, but it may be insidious in origin and subtle in its manifestation in older people. Careful palpation of the thyroid gland for the presence of a diffuse or nodular goiter should be done in all cardiac patients.

Some question continues to exist as to whether the hyperthyroid state alone can cause heart failure without preexistence of heart disease. The weight of evidence seems to indicate that hyperthyroidism, especially when it has been prolonged and is associated with rapid atrial fibrillation, can produce cardiac failure. Certainly the diseased heart tolerates hyperthyroidism poorly, even if the thyroid overactivity is relatively mild. Consideration should be given to the possibility of hyperthyroidism in all cases of cardiomegaly, atrial fibrillation, and resistant heart failure, particularly in women more than 50 years of age. The diagnosis is confirmed by chemical and isotopic studies, but at times a battery of more than one type of laboratory study is needed. Adequate therapy is generally followed by prompt improvement in the congestive heart failure state.

RENAL AND ELECTROLYTE PROBLEMS

Improvement in the understanding of the biochemistry and physiology of body fluids can contribute to therapy if alteration in these media exists in congestive heart failure. Knowledge in this field also makes it possible to avoid some of the devastating electrolyte problems which evolve from ill-advised or too energetic treatment. Problems in renal function and electrolyte abnormalities have become commoner with the successful assault on edema by potent diuretics used in conjunction with a low-sodium diet.

An electrolyte pattern of hyponatremia may ensue in patients with edema, even in the face of increased total body sodium. True sodium depletion can occur with prolonged restriction of salt and overuse of diuretics, especially in the patient with chronic renal disease. Signs of reduced body sodium are generally those of circulatory collapse, while signs of water intoxication resulting in hyponatremia are often muscle twitching and irritability. Measurement of urinary sodium excretion may be helpful in distinguishing hyponatremia of treatment from that which occurs with renal disease associated with loss of salt. Generally, large amounts of sodium appear in the urine in so-called salt-losing nephritis, while the urine has a low content or absence of sodium ion when there has been retention of this ion secondary to congestive heart failure. Restriction of water and a temporary withholding of diuretics may be necessary if decreased total body sodium is suspected in patients with edema.[5]

Peritoneal dialysis has a limited place in treatment for the patient with refractory heart failure who has disturbed renal function and an abnormal electrolyte picture. This has been shown to be a procedure by which quantities of edema fluid can be removed by peritoneal lavage with hypertonic glucose solution. Spontaneous diuresis may be initiated, and problems of hyponatremia and hypokalemia, as well as the retention of nitrogenous wastes, can be rectified or improved by this technique.[6] From a practical standpoint, the main value of peritoneal dialysis in the patient with congestive heart failure is its use in the occasional patient who has a correctable mechanical defect. This technique may be helpful in preparing the patient so that he can be brought to the operating table.

Potassium-ion depletion in patients with congestive heart failure owes its occurrence usually to overly enthusiastic diuretic treatment without potassium-ion replacement. The thiazide drugs, which are often strongly kaliuretic, are culprits in this electrolyte disturbance, especially if their use is not carefully supervised. Development of the aldosterone antagonist, spironolactone, offers a drug whose actions in preserving potassium ion, while still being an effective diuretic, may well reduce the incidence of hypokalemia in the future. It is generally used concomitantly with thiazides and has generally enhanced loss of sodium and water without inducing hypokalemia.[7]

Hypochloremic acidosis, with or without potassium-ion depletion, is not unusual and often appears in an apparent refractory edema. The patient's responsiveness to diuretic drugs usually follows promptly the use of ammonium chloride. This drug may even be used intravenously in certain situations, but this is rarely necessary.

THROMBOEMBOLISM IN HEART FAILURE

The occurrence of venous and arterial thromboses is high in congestive heart failure. Circulatory stasis and increased venous pressure and distension, as well as lack of efficiency of the muscular pump, are probably significant reasons for the high incidence. The use of passive exercises and elastic bandages on the extremities and prompt institution of anticoagulant drug treatment in susceptible patients contribute to prophylaxis against the occurrence of venous thrombosis in patients with congestive heart failure.

The development or aggravation of heart failure as a result of embolization of the lungs from peripheral sites also must not be overlooked. This complicating factor in the patient with heart failure may be difficult to establish because venous thromboses in the legs may go unnoted in the presence of edema or the emboli may have arisen from the chambers of the right side of the heart. Occurrences of embolization over a period of months give a poor prognosis. It is particularly disheartening when arterial emboli cause paralysis, loss of an extremity, or other serious complications in patients with rheumatic heart disease whose congestive heart failure might be cured or satisfactorily palliated with surgical treatment.

The clinical picture of recurrent pulmonary emboli in patients with congestive failure, especially in the absence of a major embolus, may be nonspecific and difficult to diagnose. Consideration should be given to multiple pulmonary emboli when, in the presence of congestive heart failure, there is unexplained fever, tachycardia, progressive dyspnea, and unexplained cough in spite of good diuresis.[8] Suggestive physical findings include increasing loudness of the pulmonic second sound and an increase in palpable right ventricular heave if pulmonary hypertension and right ventricular dilatation have occurred. X-ray findings of increased size of the right ventricle, increased prominence in the pulmonary artery, and translucency of the affected side with heavier markings on the opposite side may be helpful and suggestive signs. Occasionally, X-ray evidence of an overt pulmonary infarct is seen.

It should be emphasized that this factor of thromboembolism contributing to a refractory state of congestive heart failure must be considered in order to be diagnosed. Anticoagulant therapy applied during active diuretic therapy for heart failure has prophylactic value and has therapeutic value when thromboembolism is suspected or is diagnosed. It would appear that anticoagulant treatment has greater justification in the patient with congestive heart failure on a prophylactic basis than it has in a patient who has myocardial infarction without congestive heart failure.

PREGNANCY AND HEART DISEASE

A generally pessimistic attitude has prevailed for the pregnant woman with a cardiac defect that may have caused the congestive heart failure syndrome. The inherent threat to two lives troubles the conscientious physician doubly, but, fortunately, statistical studies in this field are reassuring. Rheumatic heart disease continues to be the most frequently encountered cause of heart failure in pregnant women. In the study by Burwell and Metcalfe[9] of 503 pregnant cardiac patients, a gratifying maternal mortality rate of only 1% was encountered. Death occurred among patients who were functionally in class III or IV before pregnancy.

Certain physiologic changes occur during pregnancy which are factors in producing heart failure in patients who have been found to be otherwise in a compensated state. Increased oxygen consumption, increased plasma volume, and increased cardiac output occur. These physiologic factors increase or stabilize at about the seventh or eighth month and at this point begin to regress. The pregnant cardiac patient, therefore, has some proved cardiac reserve at term.

The presence of heart disease in the pregnant woman justifies careful attention to measures to prevent cardiac overload and, thus, to prevent or to control congestive failure. Control of the patient's activity, allaying her emotional strains, and avoidance of ectopic rhythms, obesity, anemia, infections, hypertension, and other disease processes will add to an encouraging prognosis. The occurrence of episodes of acute pulmonary venous hypertension which produce nocturnal dyspnea and hemoptysis during the first trimester in patients with stenotic valves justifies surgical relief of these stenotic valves if operation can be accomplished during the first five months of pregnancy. In general, however, the pregnancy can be permitted to go to term with vaginal delivery in the great majority of patients who have associated heart disease. Pregnancy also causes little permanent or irreversible deterioration of the prepregnancy cardiac status.

COMMENT

Congestive heart failure is a symptom complex with varied etiologic aspects. Problems which arise in satisfactory management of this symptom complex can be caused by incomplete diagnosis and complications of treatment as well as by complicating extracardial influences of infectious, endocrine, vascular, and renal origins. A strong plea can be made for understanding the morbid pathology and physiology of the primary cause of heart failure, for initiating proper treatment at the proper time, and for avoiding pitfalls which lead to intractability. The potential of effective drugs to worsen the clinical state by overshooting the therapeutic range for both digitalis and diuretics also can lead to intractability. Management of congestive heart failure, therefore, is a continuing diagnostic exercise in which the clinician must be aware of subtle as well as overt influences that require adjustments in the program in order to avoid disastrous complications.

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ANAEROBIC INFECTION should be suspected in patients with sudden, overwhelming sepsis after elective abdominal surgery. Early recognition and treatment are vital when gas gangrene develops, but the pathognomonic sign of gas infiltration into subcutaneous tissue appears late, if at all. Signs and symptoms include restlessness, mental confusion, muscular pain, hypotension, tachycardia, fever, foul odor, scrotal edema, subcutaneous emphysema, abdominal tenderness or distension, skin discoloration, and cellulitis of the abdominal wall. Of primary importance is the immediate debridement of wounds and areas of cellulitis. Specific antitoxin and possibly antibiotic therapy may help. Serum therapy is equine antitoxin, each dose containing 10,000 international units of Clostridium perfringens antitoxin and 10,000 of C. septicum antitoxin. If the first injection of 20,000 to 60,000 units or more is not effective, supplementary injections of 20,000 units each should be administered at four- to six-hour intervals. Antibiotic therapy consists of crystalline penicillin in doses of 20 to 40 million units intravenously every twenty-four hours; streptomycin, 0.5 gm. intramuscularly twice daily; and chloramphenicol, 3 to 4 gm. every twenty-four hours, administered part intravenously, part intramuscularly. Hyperbaric oxygenation increases the oxidation-reduction potential, but apparently is effective only if surgical debridement has been thorough.

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Rehabilitation in Hemiplegia

MILAND E. KNAPP, M.D.
Minneapolis

THE REHABILITATION of the hemiplegic patient should begin immediately upon admission to the acute hospital, even before the threat to life has subsided. Two procedures should be instituted at once. These are bed positioning and range of motion exercises. They do not need cooperation on the part of the patient and are very simple to institute. Yet if they are neglected for a sufficient period of time, contractures and decubiti may result, which will prolong the patient's hospitalization and interfere greatly with his eventual recovery.

The bed should be prepared properly before the patient is first placed in it. It consists of an ordinary hospital bed with a plywood board covering the entire surface of the bed. Upon this is placed a felt mattress or a firm sponge rubber mattress; a compression ratio of 34 lb. to the square inch is desirable. An innerspring mattress is not satisfactory because it tends to allow the hips to sag and produce hip flexion deformity. A footboard is used which is separated from the end of the mattress by 4-in. wooden blocks. This allows the heel to be placed over the end of the mattress to distribute the weight of the leg on the entire calf instead of localizing it on the heel. The footboard thus not only prevents foot drop but also prevents calcaneal decubiti. The usual method of using cotton doughnuts and other devices is much less satisfactory because of the well-known tendency for these devices to slide around to the dorsum of the foot where they are useless.

Contractures of all joints may be prevented by carrying them through a full range of motion at least once daily. This may take some of the nursing personnel's time, but it is well worthwhile if it prevents later complications.

Prevention of decubiti is accomplished by this type of positioning and also by assuming a side-lying position on either side alternately. If the patient is unconscious or the area is anesthetic, the position should be changed at least every two hours, day and night. An alternating pressure mattress may be used to help prevent pressure sores in an individual who is usually prone to develop such complications, but position change should still be carried out regularly. When possible, the prone position should be used for a half-hour or more per day in order to overcome pressure and also to produce hip and knee extension. The spacing of the footboard from the bottom of the mattress allows the sole of the foot to be placed against the footboard without pressure against the toes when prone.

The usual hemiplegic contractures in the lower extremity consist of external rotation and flexion at the hip, flexion or sometimes extension at the knee and contracture of the heel cord. These are prevented [1] by placing the foot against the footboard as mentioned before, [2] by using a trochanter roll, which is merely a towel tucked under the hip and then rolled up under the trochanter to point the toes directly upward, thus maintaining a midposition, and [3] by using the previously described bed, which prevents hip and knee flexion contractures.

In the upper extremity, the usual contractures are adduction and internal rotation of the shoulder, flexion at the elbow, and flexion of the wrist and fingers. These are corrected by propping the arm at a right angle from the body with a pillow, supporting the forearm in a midposition with the pillow, and inserting a hand roll to assist wrist dorsiflexion and maintain a midposition of the fingers. This hand roll is merely a washcloth which is rolled up and fastened with adhesive tape. In addition, the arms should be placed in as extreme external rotation as can be tolerated by bringing the hand toward the head of the bed and supporting it there with a pillow as tolerated. Extending the elbow at intervals during the day will prevent flexion contracture. These last two positions are not easy for the patient to maintain over long periods of time, but it is important that they be assumed for short periods daily.

MILAND E. KNAPP *is clinical professor of Physical Medicine and Rehabilitation, University of Minnesota, Minneapolis.*

When spasticity begins to develop, which usually occurs within a week to ten days after the stroke, hot packs may be used to prevent the development of contractures if the patient is conscious and has heat sensation present. When the patient is cooperative, reciprocal motion may also be used; the affected arm is fastened by a wrist sling to a rope which passes over a pulley above the bed and down to a handle which he may manipulate with his good hand. Thus, the motions of abduction and flexion of the shoulder may be carried out passively by the patient himself. The same procedure may be used with the lower extremity to help prevent contractures in that area as well.

Another important consideration is the stimulation of the mental processes of the patient. Too often one sees the individual lying in bed in a very expensive hospital room, with beautiful drapes over the windows, wooden furniture, the most expensive type of bed and auxiliary equipment, and sometimes even a special nurse; but the patient lies facing the wall, the curtains are drawn, the room is dark, the only light in the room is on the nurse's book, and the patient is vegetating. To my mind, this is poor treatment. I would prefer to have the patient in a multiple-bed ward where he will be stimulated by his neighbors, even though this stimulation may result only in controversy between them. This controversy often extends to the nurse, the floor supervisor, the superintendent of the hospital, and thence to the doctor, where pressure is placed on him to put the patient in a private room. Not only is the patient stimulated, but also the physician. Nevertheless, I think the best treatment is the stimulation of mental processes in any way possible.

As soon as it is feasible, the patient should be taught as many of the activities of daily living as he can carry out in his bed or his room. This includes washing face and hands, combing hair, brushing teeth, dressing, transferring to a wheelchair, and so forth. It may be necessary to do these routines one-handed, but they can be taught to most patients.

Ambulation training will also follow as soon as practical. The patient can usually stand a very few days after onset, bearing weight on the good leg. We also try to start gait drills, consisting of bearing weight on the bad as well as the good leg, bending each knee alternately, and transferring weight. Of course, somebody must be present to be sure that the patient doesn't lose balance and fall. When it is deemed that he is ready for ambulation, he starts taking steps, first in the parallel bars, then in a walker or with crutches, then with a cane, and eventually, hopefully, with no assistance at all.

Many of these patients require a foot-drop brace, not so much to prevent foot drop as to prevent the inversion of the foot which so commonly accompanies the spastic pattern of gait that frequently develops. This may be a temporary type of brace because, in most instances, sufficient function will return to make a stable gait possible without bracing. Very rarely is a long-leg brace indicated, regardless of weakness, because if the patient can't walk without the brace, it is my experience that he usually can't walk with it, and, thus, it is an unnecessary expense.

CONSERVATIVE MANAGEMENT of malignant melanoma of the superficial dermis carries excellent prognosis. Lesions, usually less than 1.5 cm. in diameter, are treated by wide excision and primary closure. In 24 of 48 patients with malignant melanoma, lesions were superficial. Follow-up of the 24 for at least two and a half years revealed local recurrence in 3 and cervical lymph node metastasis in 1. No deaths occurred from malignant melanoma.

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RUTH E. BOYNTON *Series*

The Continuing Menace of Tuberculosis for Children

EDITH M. LINCOLN, M.D.
New York

In general there is a direct relation between the amount of active tuberculosis in any geographic area and the socioeconomic level of the inhabitants. Wherever living conditions are poor and diet is inadequate it is usual to find more tuberculosis than in areas where the standard of living is higher. For this reason tuberculosis is more common in developing countries and in crowded slums of large cities. In those countries where public health control of the disease has been attempted for many years, the death rate of children from tuberculosis began to decline long before specific therapy was available. It is impossible to single out any one factor which was responsible for the decline in the death rate between 1930 and 1945. We cannot say that it was due to Bacillus Calmette-Guérin (BCG) vaccine because the death rate also fell in a similar manner in countries where it was not used widely. In part the fall in death rate must have been due to the decrease in tuberculosis of cattle and the consequent lessened danger of milk as a source of infection. The improvement in health conditions due to the antituberculosis campaigns also must have had an influence on the death rate.

With the introduction of specific therapy with streptomycin a sharp decline in the death rate from tuberculosis in children occurred in many European countries. This is shown for the Scandinavian countries, England, and Wales in figure 1. It will be noted that the precipitous decline of the death rate in the United States began three or four years later than in the northern European countries. Physicians in this country were at first very sceptical of reported cures of miliary tuberculosis and tuberculous meningitis and consequently during the early years of chemotherapy, treatment of many patients was not as intensive as it should have been. At the present time the death rate is of diminished epidemiologic significance for tuberculosis control because of the almost universal acceptance of drug therapy. The rate of tuberculous infection and the rate of active disease in children are much better measures of the extent of the problem than the death rate.

The reported active case rate for tuberculosis has declined markedly but the rate of decline in adults is much more marked than in children as shown in figure 2. Unfortunately the active case rate in children does not reflect conditions as well as it does in adults. Standards for reporting have not been established and in some areas conversions of tuberculin tests with negative roentgenograms are reported as active tuberculosis, while in other sections only children with roentgen evidence of tuberculosis or extrapulmonary complications are reported. Registries should be established which will distinguish between tuberculous infection, for example, a positive tuberculin test without other evidence of tuberculosis, recent conversion of the tuberculin test with negative roentgenograms, and pulmonary primary tuberculosis, with and without calcification. In addition, all complications such as meningitis or cervical adenitis and chronic pulmonary tuberculosis would, of course, be reportable. Such registers would be a great aid to accurate estimation of the extent of the problem of tuberculous infection in children and would also be of help in focusing attention on the areas of greatest concentration of tuberculosis in adults. The task of organizing and maintaining a good tuberculosis register is a very difficult one and it is essential that a system should be devised that not only would assure accuracy but maintain

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EDITH M. LINCOLN *is with the Department of Pediatrics, New York University Medical Center, N.Y.*

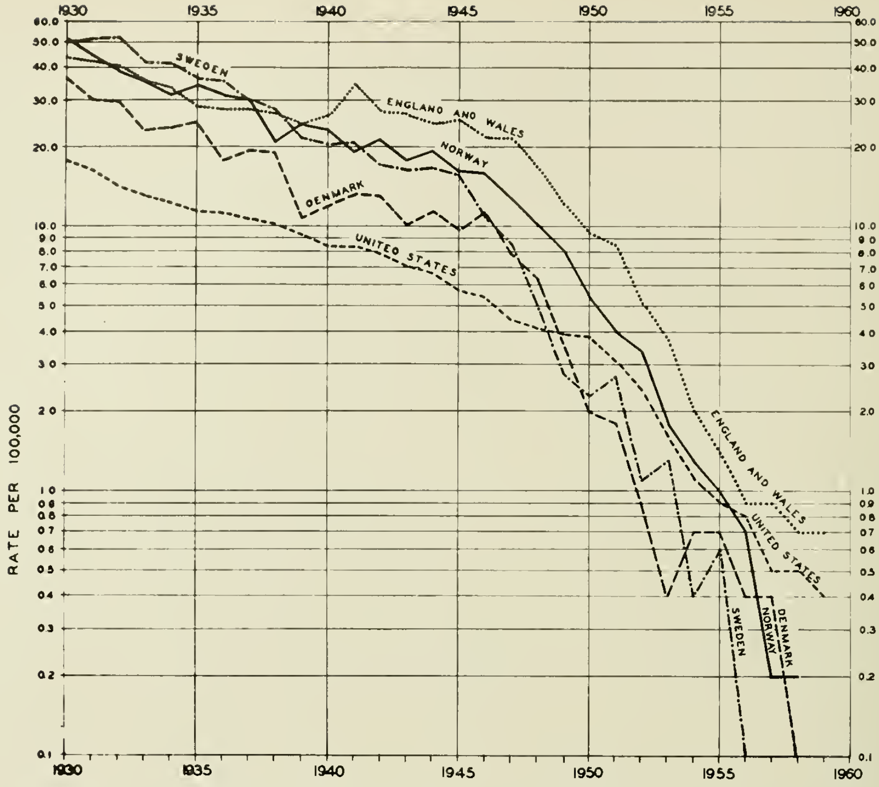

Fig. 1. Decline in death rates for children in Scandinavian countries, England and Wales, and United States, 1930-1959. In United States death rate did not begin to accelerate until 1950. Rates for Sweden for 1957-1959 and for Norway and Denmark in 1959 are not shown on chart because they are insignificant. There were 3 deaths in Denmark, 2 in Sweden, and none in Norway in 1959. (Adapted from Drolet, G. D., and Lowell, A. M., and reprinted from Arch. Environ. Health 3:444, 1961)

current information while eliminating outdated material. If adequate registers were maintained, data regarding the annual rate of infection in different age groups would be available and such information could determine how effective the tuberculosis control program was and whether special preventive measures were indicated. Well kept registers not only would be of great value locally but would also increase knowledge about trends of tuberculous infection and disease if all data collected could be analyzed by a single computer and so give comparable information for the entire United States.

PREVENTION OF TUBERCULOUS INFECTION IN CHILDREN

The first line of defense against infection of children with tubercle bacilli consists in keeping them away from contact with individuals who have contagious tuberculosis. This is accomplished in part by health departments through prompt diagnosis and treatment of adults with active disease. Good initial treatment results in a high rate of rapid sputum conversion and reduces the danger of spread of the disease. Unfortunately, as has been shown repeatedly, many child contacts have already been infected by the time the source case is identified. Examination of the contacts of newly discovered tuberculous adults is the case finding method which uncovers the largest number of children with primary tuberculous infection. A recent field study of the United States Public Health Service was conducted among more than 25,000 household contacts of newly reported cases of active tuberculosis. The majority of the contacts were children, and 2.1% were found to have primary tuberculosis.

To prevent infection of these household contacts methods would have to be developed to diagnose pulmonary tuberculosis in the source case before it became contagious. The United States Public Health Service estimate of the origin of future cases of tuberculosis is seen in figure 3. It was anticipated in 1960 that at least 3 out of 4 future cases would occur in individuals already infected. If registries were established for all ages, not only for active cases but for all

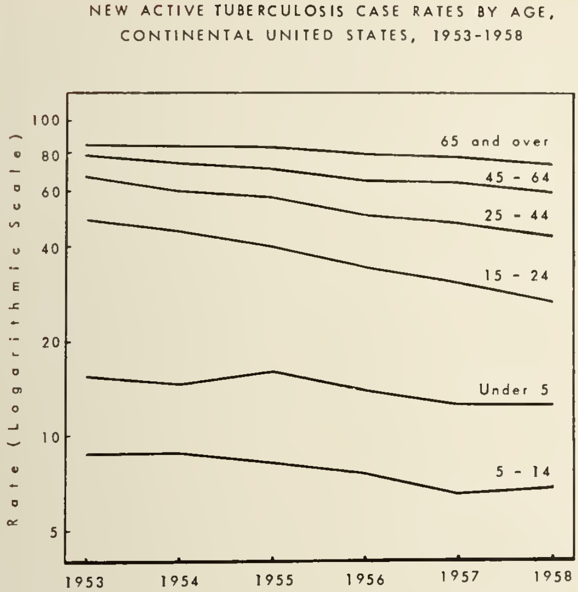

Fig. 2. New active case rates by age in continental United States, 1953-1958. Rates for children have decreased less than those for adults. (U.S. Department of Health, Education, and Welfare, Public Health Service, Tuberculosis Program)

persons with positive tuberculin tests, and a real effort made to take yearly roentgenograms, undoubtedly many more diagnoses of active disease in adolescents and adults would be made before child contacts were infected.

Another method used by health departments to prevent tuberculous infection in children is the requirement of a yearly examination of all adult personnel in schools. This rule should apply to all types of schools, including nursery and Sunday schools and private and public schools. Teachers, bus drivers, cooks, or other members of the maintenance staff should be examined before they are permitted to work, regardless of whether they are employed on a full-time, part-time, or temporary basis, or whether they do paid or volunteer work. A tuberculous teacher is very apt to infect children because her work, especially with young children, involves close contact and droplet infection can occur easily. As the rate of tuberculous infection declines the percentage of children susceptible to infection with tubercle bacilli increases and school epidemics may be more likely to occur. Probably many are unrecognized at the present time since primary tuberculosis so often is free from symptoms and not recognized unless complications occur or a program of annual tuberculin tests discloses an increased number of reactors. A recent survey disclosed a number of reports of outbreaks of tuberculosis in schools in Europe, Canada, and the United States. Seventy school epidemics were found that had occurred since the introduction of chemotherapy for tuberculosis. Most epidemics were traced to teachers and occasionally to other members of the school staff to whom the children were exposed. In 1961 Mahady reported an outbreak of primary tuberculosis in a group of school children in New York state who had been exposed to a tuberculous bus driver. The tuberculin reaction rate for the chil-

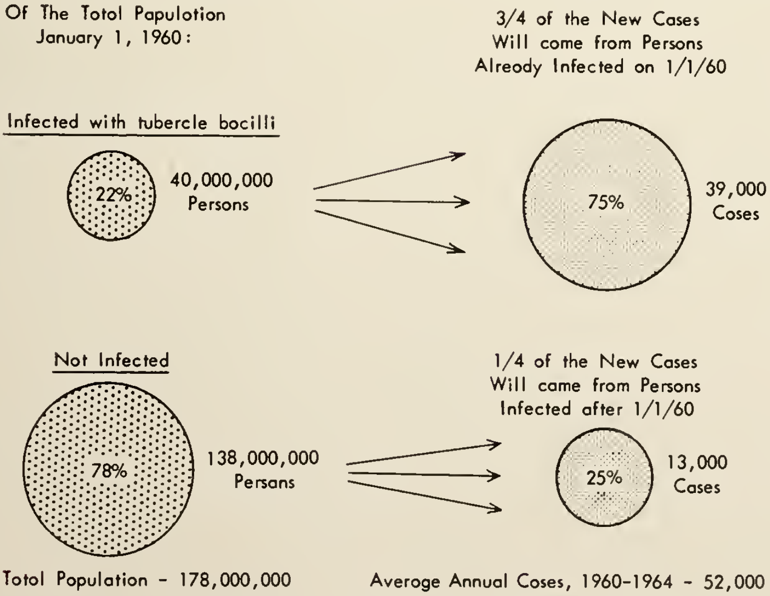

Fig. 3. Origin of future tuberculosis cases. It is anticipated 3 out of 4 future cases will develop among persons already infected. (U.S. Department of Health, Education, and Welfare, Public Health Service, Tuberculosis Program)

dren who did not ride on the bus was only 1.8% and the rate for active tuberculosis 0.1%. On the contrary, 36% of the children who rode on the tuberculous driver's bus showed skin reactions to tuberculin and 19.5% of the group had roentgen evidence of primary tuberculosis.

In a smaller number of epidemics the source was an older child or adolescent with chronic pulmonary tuberculosis. Yearly tuberculin testing of all negative reactors and roentgenograms of all who react should uncover many of these cases while the danger is still potential. A scheme to stimulate such programs was proposed by the American School Health Association in 1940 and has been endorsed by Dr. J. A. Myers. A certificate is awarded to each school that examines every member of its adult staff yearly and does yearly tuberculin tests on 95% to 100% of all students not known to be reactors, followed by roentgenograms of reactors. All reactors must have physical examinations to exclude evidence of extrapulmonary tuberculosis. Continuous records must be kept for all persons tested and all reactors must be followed and reported to the health department. An educational program on tuberculosis and tuberculin testing is required to make sure that the teaching staff, students, and parents understand the underlying principles of tuberculosis control. Many thousands of schools, chiefly in the Middle West, have been accredited and an extension of this plan throughout the United States would seem desirable.

Parents and guardians have a distinct responsibility to protect the children in their care from exposure to persons with contagious tuberculosis. While the threat of infection is greater to children living in crowded homes, especially in areas where there is a high incidence of tuberculosis, many children who are well housed and well fed contract tuberculosis each year. No one should be allowed to care for a small child or even to work in the same household unless he or she has been screened for tuberculosis. In homes of good economic level the source of infection is often a sitter, maid, or nurse, whereas in less affluent homes tuberculous infection is more often traced to a member of the family or to a boarder. The likelihood of infection varies with many factors but the possibility is always present when a susceptible child is exposed to an individual with contagious tuberculosis even for a short time.

The individual physician should never forget that it is part of his responsibility to guard children from infection with tubercle bacilli by education of tuberculous patients and their families and by warning parents of young children of the possibility of tuberculous infection through exposure to helpers in the household whose health status has not been checked.

Prevention of tuberculous infection in children also may be accomplished by vaccination or by administration of isoniazid for so-called primary or infection prophylaxis. When properly done with well standardized material, vaccination with the BCG strain of attenuated bovine bacilli produces an immunity to infection with human tubercle bacilli which lasts for an uncertain time but usually protects an infant during his most susceptible years. When and if superinfection with human bacilli occurs, the risk of progressive disease and of serious complications is markedly diminished. Primary infection also can be prevented by administration of isoniazid as has been demonstrated in field studies of the United States Public Health Service. About 30,000 household contacts of cases of active tuberculosis were followed and one-half of the individuals were given isoniazid for a year and the others were given placebo which was identical in size and taste. A statistically significant larger number of those receiving placebo became infected with tubercle bacilli than of those receiving isoniazid.

No investigators have claimed uniformly good results with either method of prevention of infection. Moreover, it would be impossible to secure 100% cooperation in accepting either drug or vaccination. The British claim that BCG vaccination was more than 80% effective and the United States Public Health Service makes a similar claim for isoniazid prophylaxis. However, in areas with a low rate of infection neither method is desirable because such a large percentage of the children receiving preventive measures would not be at risk of infection. Arvid Wallgren, who for many years has been an ardent proponent of BCG, stated in 1959: "If the infection rate falls to below 10% at puberty the use of BCG vaccination, except in known contacts, becomes debatable." Neither BCG nor isoniazid prophylaxis would eliminate the need for follow-up of all the children, because of the number who either did not avail themselves of the preventive method or in whom it was not successful. Vaccination or the use of prophylactic isoniazid may be advisable in countries where the infection rate is still high and in isolated areas in the United States, as on Indian reservations or in sections of large cities where control programs have failed to reduce the infection rate in children.

An epidemic reported by Warfvinge in 1960 illustrates a point that Wallgren has repeatedly emphasized, that BCG is not as effective in preventing reinfection tuberculosis as in preventing primary tuberculosis. Since 1940, 90% of the population of Lapland was vaccinated at birth with BCG and some had been revaccinated at school age because they had negative tuberculin tests. The contacts of a 19-year-old man with pulmonary tuberculosis were examined and 27 people had tuberculosis. Primary pulmonary tuberculosis was diagnosed in 2 persons who had never received BCG vaccination. Twenty-two individuals, of whom 19 had been vaccinated, had pleurisy with effusion and 3 who had received BCG had pulmonary tuberculosis.

The physician in clinic or private practice must consider the need for vaccination or chemoprophylaxis on an individual basis. Some method of prevention is desirable when a child, especially an infant, has to remain in an environment where the risk of infection is high. BCG should be given if tubercle bacilli from the potential source case have shown drug resistance. It is not necessary nor desirable to vaccinate every household contact of a patient who is receiving drug therapy at home. In general the risk of contagion is slight. Aside from the number of tubercle bacilli in the sputum, there is a great variation in the contagiousness of individual patients. When the potential hazard of exposure is of short duration, as when a tuberculous grandfather, or one suspected of tuberculosis arrives for a brief visit, chemoprophylaxis should be the method of choice.

Prophylaxis with isoniazid has the disadvantage that pills have to be taken and this means supervision by physician or public health nurses, but it has the advantage that it does not produce a skin reaction to tuberculin and thus interfere with the diagnostic value of the tuberculin test. This is one of the main charges against the use of BCG and it is disputed by many proponents of vaccination. They claim that they can distinguish between a positive Mantoux due to BCG and one due to natural infection with human tubercle bacilli. It is true that many children after BCG vaccination have small (less than 10 mm.) reactions to 5 tuberculin units of purified protein derivative (PPD). However, it is also true that skin reactions of infants infected with human tubercle bacilli tend to be much smaller than those of older children similarly infected. An infant who has been vaccinated with a resulting small reaction to tuberculin and later develops a marked reaction almost invariably has been superinfected with human tubercle bacilli. This was demonstrated by Wallgren long ago. But if one has no knowledge of the previous vaccination and only knows that the child has a positive tuberculin test and a chest roentgenogram within normal limits, few physicians can distinguish, by the character of the test only, between the diagnosis of minimal primary tuberculous infection and skin hypersensitivity due to BCG vaccination.

This may seem a trifling point but it is very important. For the infant with an infection due to human tubercle bacilli is at a minimal, but definite risk of tuberculous meningitis unless treated with isoniazid for a year. On the other hand, isoniazid should be avoided in an infant who has recently been vaccinated because bovine bacilli are susceptible to isoniazid and the drug might counteract the value of the vaccination.

PREVENTION OF COMPLICATIONS IN TUBERCULOUS CHILDREN

In areas with a low rate of infection any interference with interpretation of the tuberculin test is inadvisable because of the great value of the test in selecting children for disease prophylaxis with isoniazid. Arvid Wallgren agrees that in areas of low incidence of tuberculosis "The loss of the tuberculin test for diagnosis of tuberculous infection is a strong argument against the introduction of a more general BCG vaccination program." Most patients with primary tuberculosis discovered on contact examination or by periodic tuberculin testing are free from symptoms, and complications in such cases can, almost invariably, be prevented by the administration of isoniazid daily for a year—so-called disease prophylaxis. The Tuberculosis Meningitis Prophylaxis Study of the Public Health Service demonstrated conclusively that the administration of isoniazid for a year to children with tuberculous infection markedly diminished the risk of complications including meningitis. Both the British and the United States Public Health Service have shown that tuberculin reactors, excluding those due to vaccination, are at a much greater risk of developing tuberculosis than nonreactors. In areas where the infection rate is low it should be possible to keep the reactors under observation and treat them if necessary rather than to cause conversion of the tuberculin test to positive in a large percentage of the children by BCG vaccination, thus making it difficult to identify those who are at the greatest risk of developing chronic pulmonary tuberculosis.

There does not seem to be an adequate reason why children in any community cannot be tuberculin tested periodically. In infancy attempts are made at present to vaccinate all children against smallpox, tetanus, diphtheria, whooping cough, measles, and poliomyelitis. The same health authorities who are responsible for these preventive measures could also do biyearly tests on small infants and yearly tests after the age of 2. Physicians in private practice and in clinics should be encouraged to do the same and to repeat tests when there is the faintest suspicion of tuberculous infection.

Because of the prevalence in the southeastern states of small tuberculin reactions in children that are due to infection with atypical acid-fast bacilli, it would be desirable in this area to accept only Mantoux tests, but experience has shown that relatively few physicians are prepared to do many Mantoux tests either in private or clinic practice. Since the aim of a control program is to secure as many tests as possible, it is better to encourage the use of qualitative tests such as the Heaf and tine tests for screening. A Mantoux test with 5 tuberculin units of PPD should be done in all cases where the qualitative test is considered positive and the chest roentgenogram negative. Whenever possible a simultaneous test with PPD-B should be given or Mantoux tests with other antigens made from atypical bacilli which are locally prevalent. Undoubtedly, different standards for a positive tuberculin test must be accepted in different geographic areas. In New York, induration of 8 to 10 mm. or more can usually be accepted as evidence of M. tuberculosis infection when 5 tuberculin units of PPD are injected. Smaller areas of induration often reflect cross reactions to other mycobacteria. In Alaska, where atypical acid-fast bacilli are rare, some authors believe that any amount of induration, no matter how small, is evidence of a tuberculous infection. In some southeastern states 12 mm. of induration have been suggested as minimum evidence of a tuberculous infection. It is obvious that for analysis by a computer all tests should be recorded by measurements of induration and never just as positive or negative. If qualitative tests are to be accepted in areas of high prevalence of sensitivity to antigens of atypical mycobacteria, standards for their interpretation and provisions for checking with Mantoux tests must be established. Materials for testing should be made available, free of charge, for physicians willing to join in the program of tuberculin testing.

Although periodic tuberculin testing of all children does not uncover as many infections as examination of children who have household contacts, it often establishes the diagnosis of tuberculosis in children who have no history of exposure to tuberculosis. As the goal of eradication of tuberculosis is approached there will be fewer adults with tuberculosis and more tuberculin tests will be needed to find infected children. The only way to identify them is by the tuberculin test.

Most of the menace of tuberculosis for children could be eliminated if parents and physicians and all who are responsible for children would recognize the potential danger of exposure of young children to adults whose health status is unknown. At the same time the value of frequent tuberculin testing should be acknowledged as the best means of diagnosis of infection with tubercle bacilli. A conversion of the test to positive should be the signal for immediate prophylactic treatment with isoniazid.

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The Management of Acute Asthma

HADDON M. CARRYER, M.D.
Rochester, Minnesota

Each physician should have clearly in mind those measures to be undertaken when he must direct the treatment of acute asthma. His capacity to deal with this medical emergency may indeed prove to be lifesaving. While there may be variations of emphasis and of philosophy in the management of chronic asthma, there are few differences in the things to do for the acutely ill asthmatic patient.

SYMPTOMATIC RELIEF

A bronchodilator such as epinephrine is the first drug considered in the management of the acutely ill asthmatic patient. It should be given in sufficient doses and with sufficient frequency; inadequate and delayed use of epinephrine is responsible for more harmful results than is its excessive use. While some patients have relative contraindications to the use of epinephrine—old age, vascular disease, and hypertension—it is also true that severe asthma produces greater stress than does the small amount of epinephrine which usually affords prompt relief. Epinephrine should be administered early in an attack of asthma; undue delay leads to the need for larger and more frequent doses.

Epinephrine is most effectively administered by hypodermic injection of 0.25 to 0.5 ml. of a 1:1,000 aqueous solution. I prefer to give a series of smaller doses, repeated at intervals of from twenty to thirty minutes. An aqueous solution may be preferable to oil or other vehicles designed to prolong the action. Such agents retard absorption when epinephrine is urgently needed. Moreover, they allow the absorption of epinephrine when it may be less urgently needed. I believe that the asthmatic patient should be instructed in the self-administration of epinephrine. If he knows that he must call someone else—a physician, a nurse, or a relative—to give epinephrine, he meets an attack of asthma with far greater anxiety. It is as logical for the asthmatic patient to give himself epinephrine as it is for the diabetic patient to be instructed in the self-administration of insulin.

Nebulized solutions of epinephrine may be used in concentrations ranging from 1 to 3%. Some patients prefer this form of medication. A widely used modification of epinephrine is isoproterenol. This is used primarily by nebulization, either with a hand-operated nebulizer or from pressurized containers which may be carried in a pocket or purse. These solutions are 0.25 to 0.5% in a finely dispersed state and, when they are deeply inhaled into the lungs, usually afford prompt relief. Isoproterenol for sublingual use is a relatively weaker drug and is effective in only minor asthmatic episodes. For nebulization I usually prefer isoproterenol to epinephrine.

For the acutely ill asthmatic patient, ephedrine given by mouth affords a sustained bronchodilating effect. Twenty or more minutes may pass before effective amounts may be absorbed; however, the effect of the drug extends from four to six hours. The usual dose is 24 mg., administered every four hours. Most commonly, ephedrine is combined with sedatives and xanthine drugs. Unfortunately, some patients tolerate ephedrine poorly. They experience undue cerebral excitation, cardiovascular symptoms, or, among elderly men, urinary obstruction. Intolerance may limit the value of ephedrine in the management of asthma. If this occurs, the use of other related drugs, such as methoxyphenamine (Orthoxine®), may afford adequate relief.

A most important group of drugs is the family of xanthine derivatives. Of these, aminophylline is used perhaps more than others. It is most effective when administered intravenously, but oral or rectal administration is also of value. Aminophylline is administered in amounts of 0.25 gm., usually added to intravenous fluids. Occasionally, with a critically ill patient, it is necessary to inject the entire contents of an ampule (10 ml., 0.25 gm.) directly into the vein. Should this be necessary, the drug should be injected very slowly. With severe asthma, additional injections of aminophylline may be made into the tube of a freely running intravenous setup.

HADDON M. CARRYER *is with the Section of Medicine, Mayo Clinic, Rochester, Minnesota.*

Aminophylline in 0.5-gm. rectal suppositories or as a powder dissolved in retention enemas affords relief. This mild yet prolonged antiasthmatic effect of aminophylline when used at bedtime may make the difference between asthma occurring or being avoided during the night. Unfortunately, aminophylline is somewhat irritating to rectal mucosa and, on occasion, perianal or rectal irritation prevents its use. Orally administered aminophylline is less beneficial. Many patients become nauseated when receiving as much as 1.3 gm. daily of aminophylline.

HYDRATION

An important yet often neglected aspect of the management of asthma is adequate hydration of the patient. Severely ill asthmatic patients often eat poorly, perspire freely, and take only small quantities of liquids. This dehydration leads to further inspissation of the sputum, further coughing, and more bronchospasm, and it often is the basis for a vicious cycle leading to status asthmaticus.

Among the first therapeutic measures is the intravenous administration of fluid, which I keep running freely until the patient's condition is improved. During the first twenty-four hours, a severely dehydrated patient may receive as much as 5 liters of fluid, although later 3 liters daily are usually adequate. The slow administration of fluids—1 liter administered each eight-hour period—obviates multiple venipunctures. When prolonged therapy is anticipated, a plastic needle in the vein is less irritating.

Most commonly, I use 5% glucose in water. Glucose helps to provide nourishment, replenishes liver glycogen, and is isotonic. However, it is necessary that electrolytes be carefully considered when a large quantity of fluid is being administered. Sodium chloride solution should be included with approximately each third liter of intravenous fluid administered; more saline should be given if patients are perspiring freely or if vomiting or diarrhea has occurred. An electrolyte disturbance is suggested by unusual excitation, by weakness, by drowsiness, or by loss of consciousness. When these occur, or when prolonged intravenous administration of fluids becomes necessary, additional information should be obtained by electrolyte and pH studies of the blood. These values are most helpful in guiding further hydration and electrolyte therapy in the critically ill asthmatic patient. The most frequently encountered electrolyte disturbances are respiratory acidosis and water intoxication, particularly if sodium and chloride are washed out through overenthusiastic hydration. As a patient resumes the normal ingestion of foods and fluid orally, he is reasonably past the point where major disturbances in electrolyte balance are likely to be encountered.

As the patient improves and normal hydration is reestablished, intravenous administration of fluid may be discontinued. This should, however, be supplanted by an adequate oral intake of fluid to maintain hydration. We encourage the asthmatic patient to drink generous quantities of liquids. He should take at least 3 liters of fluid daily by drinking a glass of liquid each hour he is awake.

The quantities of fluid which I have suggested must be sharply curtailed if one has doubts as to the patient's cardiac reserve. Moreover, in those patients with hypertension or cardiac disease for which thiazide drugs are being administered, particular care must be exercised to avoid salt and water imbalances as one aggressively treats the acute asthmatic problem.

To each liter of fluid I usually add 0.25 gm. of aminophylline. Also, when a decision has been made to employ steroid therapy, hydrocortisone is also added to the initial 1 or 2 liters of fluid used in hydrating the patient. Sodium iodide is another additive which is occasionally used, especially in the postoperative patient; 1 gm. may be added to 1 liter of intravenous fluid once or twice daily when a patient can take no fluids by mouth, yet is developing inspissation in his bronchial secretions.

EXPECTORANTS

The use of expectorants in the management of asthma is one of the most important aspects of treatment, and yet it is one of the most commonly neglected. Expectorants make the bronchial secretions thinner and enable a patient to raise them without tiresome coughing. Expectorants make rest possible for the inflamed bronchi at a time when such rest is urgently needed. However, expectorants are of limited value unless accompanied by measures to promote hydration.

The most effective expectorant is an inorganic iodide salt. This is usually prescribed as potassium iodide, 0.3 to 0.65 gm., diluted with water and administered after meals and at bedtime. When gastric irritation is a problem, enteric-coated tablets of potassium iodide may be used. Unfortunately, many patients tolerate iodides poorly. Acne-like eruptions, swelling of the salivary glands, or other evidences of intolerance may develop in some patients. Nevertheless, I will commonly prescribe iodides for brief use because of their more effective sputum-thinning property and then change later to a less effective expectorant.

Among other expectorants which may be employed in patients exhibiting iodide intolerance are glyceryl guaiacolate and ammonium chloride. In my experience, these fall far short of iodides in effectiveness.

In recent years, several detergent and proteolytic enzyme preparations have been made available for nebulization in the management of bronchitis with tenacious secretions. In general, I have found these to be of limited value. Some patients with tenacious secretions are benefited by a face tent supplying water vapor in oxygen.

SEDATIVES

Patients who have severe asthma become profoundly exhausted, lose sleep, harbor mounting anxiety, and, therefore, become prime candidates for sedation. However, there has been increasing mortality from status asthmaticus as sedation has been used excessively in the care of patients with severe asthma. One should avoid prescribing drugs which depress the respiratory center; all opiate drugs are in this category. Likewise, one usually should avoid drugs which suppress the cough center, to protect against atelectasis.

Asthmatic patients frequently tolerate sedation poorly and, at times, will be stimulated rather than sedated by barbiturate drugs. Ataractic drugs, such as meprobamate (Miltown®) and chlordiazepoxide (Librium®), have been most helpful in sedating the asthmatic patient. Chloral hydrate is also well tolerated by the asthmatic patient.

STEROID DRUGS AND ADRENOCORTICOTROPIC HORMONE (ACTH)

The steroid drugs represent a new and powerful mode of therapy in the management of asthma; however, these drugs are but one facet of the program. They usually effect prompt control of asthma, but, with discontinuation of such therapy, the asthmatic patient is soon in difficulty again. Those patients deriving sustained benefit are often the ones who, during their brief respite from asthma, were able to control the other factors responsible for or contributing to their problem. Unless such factors are corrected, approximately half of asthmatic patients will be in difficulty within a week after steroid therapy is stopped.

Because of the problems associated with the use of steroids, they should be prescribed only for compelling indications. To discontinue use of these drugs poses a still greater problem when they have been employed over a long period. Therefore, patients who can achieve some benefit by other measures should be advised to do so. In behalf of steroid therapy, however, I must say that its judicious use has indeed been lifesaving many times—even when its use has been required over a long period. It has transformed many invalids into effective members of society.

Indications for use. I prescribe steroids for the seriously ill patient who is failing to respond adequately to other conservative measures or for the critically ill patient. Increasingly, we are faced with the problem of treating a patient who has used large amounts of steroids, has used steroids over very long periods, or has used steroids recently. In these cases, we are concerned with potentially frail adrenal function which may be inadequate in the exhausting physical effort of a severe asthma. In this type of patient, I will usually reinstitute a steroid regimen. There are certain asthmatic patients, such as those scheduled for operation for malignant disease or those with severe coronary artery disease, for whom steroids will be used because of the associated disease. A need for adequate control of cough, as in the patient with a postoperative hernia, may be a further indication for steroid therapy.

Plan of treatment. I prefer to use intermittent courses rather than a continuous program ef steroid therapy. Such courses usually extend from a few days to three weeks. When possible, I avoid the continuous use of steroid drugs because of their tendency to suppress adrenocortical function; yet, at times, their continuous use becomes necessary. Moreover, in asthmatic patients there are other classic, although relative, contraindications to the use of steroids: duodenal ulcers, tuberculosis, pyogenic infections, and emotional instability.

Preparations to use. Many steroid drugs are effective in the management of asthma, and I do not intend to recommend a specific one. I probably have used triamcinolone more than other steroids in the management of the acutely ill asthmatic patient. I have also used methylprednisolone and prednisolone extensively. Hydrocortisone, given intravenously, has been used most often at the start of a program of steroid therapy. The doses I shall mention are those to be used with triamcinolone or with methylprednisolone. For prednisolone, these doses should be increased 25% for comparable therapeutic effects.

It is important that an adequate dosage be employed. In starting steroid therapy, I commonly administer 8 mg. of triamcinolone each six hours for the first day or until evidences of improvement are noted. I then begin a rapid curtailment of steroid dosages, usually reducing the total daily dosage from 32 mg. to perhaps 8 mg. within a week. With a patient who has received steroids over a long period, the rate of decrement will be less from this point on. During the month after the patient leaves the hospital, the steroid dose would be cut from 8 mg. to 4 mg. per day. Thereafter, additional decrements should be very small, perhaps of the magnitude of 0.5 mg. to 1 mg., and should be instituted each month. Later, as the patient has tolerated cuts to perhaps a total daily dose of 3 mg., the divided daily dose is aggregated into a single morning dose. Ultimately, the entire forty-eight hour dose of steroids is administered at once. Such a program enables an earlier return to satisfactory adrenal function and allows further tapering off of steroid therapy.

I have used relatively little ACTH in the management of asthmatic patients, largely because of the inconvenience of injecting the material. Moreover, one may have doubts as to how effectively this may stimulate a flagging adrenal function. I have not found the intermittent use of ACTH to be of great help in offsetting pituitary or adrenal suppression.

GAS INHALATION THERAPY

Gas inhalation therapy, particularly the administration of oxygen, is of great importance, especially when cyanosis exists, and is indicated in the treatment of asthmatic patients who have other complicating diseases such as pneumonia, congestive heart failure, anemia, or other circumstances which interfere with the oxygenation of the blood.

The method by which the oxygen is administered may vary from patient to patient. Most commonly, I administer oxygen to the asthmatic patient by the BLB mask which may be applied or removed in accordance with changing needs for oxygen therapy. If associated conditions or a status asthmaticus requires continuous therapy with oxygen, then other measures, such as an oxygen tent, nasal catheter, or face tent, may be more suitable. When administering oxygen by a BLB mask, I usually allow a flow of 6 to 9 liters per minute. This can be judged by determining the flow which allows the proper functioning of the rebreathing bag.

Mixtures of helium and oxygen were used more frequently in the past than recently. Still, this represents one means of helping the asthmatic patient by providing a thin gas mixture. The unique physical properties of helium enable it to pass through constricted bronchial tubes with less turbulence. One should warn such patients of the high-pitched voice changes which will be noted while helium and oxygen mixtures are being administered.

If there is extensive emphysema, oxygen therapy should be used with some caution. Oxygen need may be an important stimulus to the flagging respiratory center. The sudden withdrawal of this stimulus may bring about a depression in respiratory function leading to loss of consciousness, convulsions, and other evidences of respiratory failure.

Another mixture often helpful for asthmatic patients in the postoperative period is 5% carbon dioxide and 95% oxygen; this is used by isolated inhalations. The deep breathing induced by carbon dioxide aerates the lung bases, and, for those who have had abdominal surgery, such inhalations may overcome atelectasis.

Most often, the gases are administered at the prevailing barometric pressure. There are available, however, such devices as the Bennett valve and Bird valve which provide gas therapy at pressures greater than existing barometric pressure. With pulmonary edema, such increased pressure may be lifesaving. Also, for the unconscious asthmatic patient, particularly the one in deep respiratory acidosis and coma, the breathing assistance provided by these mechanical devices becomes vital. However, we do not routinely employ such positive-pressure devices in the management of asthmatic patients.

MANAGEMENT OF BRONCHITIS

Every asthmatic patient has some degree of bronchitis associated with his asthma. Many of the treatments already considered actually have been directed toward the problem of bronchitis. If the asthmatic patient has fever, purulent sputum, or roentgenographic evidence of inflammatory changes in the lungs, it is probable that antibiotic therapy will be needed as a supplement to those measures already considered. The appropriate antibiotic is best determined after bacteriologic and sensitivity studies of the predominant organism in the sputum. It is desirable, however, to proceed tentatively with antibiotic therapy rather than to await the results of these studies. Tetracycline and erythromycin usually have been helpful. If antibiotic therapy must be administered over a long time or if the response to therapy is slow, then the sensitivity and bacteriologic studies should be repeated.

If there is no evidence of significant bacterial infection, the use of antibiotic drugs not only may be of limited value but, indeed, may be harmful. Through changes in bacteriologic flora brought about by broad-spectrum therapy, essentially harmless organisms may be replaced by virulent organisms for which no antibiotic treatment is available.

HOSPITALIZATION

Many of the procedures I have described are most readily applied to the patient who is hospitalized, and it is desirable that the patient who is seriously ill with asthma be placed in a hospital. He is thereby removed from offending substances in the home environment such as dust, feathers, and animal dander. In most hospitals the environment provides adequately filtered and humidified air. Furthermore, in the home there is always great anxiety among relatives when the patient is failing to respond to therapeutic measures, and this does not go unnoticed by the anxious patient; the prompt availability in a hospital of symptomatic relief for asthmatic paroxysms is reassuring. The asthmatic patient should be placed in a private room. Such a patient often has his greatest difficulty during the night, disturbing the rest of other patients and compounding his own anxiety. Moreover, problems in the control of other patients with their visitors, smoking, conversation, and bacteria are best avoided.

OBJECTIONABLE PRACTICES

There are a number of objectionable practices which should be emphasized because they interfere with the best care of the asthmatic patient.

1] Opiate drugs suppress the respiratory center and should be avoided. Moreover, these drugs suppress the cough center, thereby enhancing the possibility of atelectasis.

2] Too much sedation is undesirable. Medical literature is replete with studies showing that asthmatic patients are more likely to succumb when excessive amounts of sedation have been employed in their care.

3] The patient should not be exposed to the fumes of burning stramonium powder and asthma cigarettes. Although at times these afford a measure of relief, they also aggravate bronchitis and, hence, are objectionable.

4] No asthmatic patient should smoke.

5] Patients should suppress the tendency to cough excessively hard, especially after hydration has been effected.

6] Arsenical preparations should not be used. The arsenical intoxication poses a continuing hazard for the rest of the patient's life, which overshadows any benefits of the drug in the treatment of asthma.

7] Advising the patient to seek another climate, along with implied benefits of such a move, is a poor practice. Only on the basis of the patient's personal experience in a climate or community should such a change in residence be considered. Even then, moving is far down the list of therapeutic opportunities to be considered.

CONCLUSIONS

As the asthmatic patient improves and as the continued administration of medications is no longer necessary, one may investigate the ultimate reasons as to why the patient's asthma is occurring. Only then should one consider such measures as bronchoscopic studies, intranasal surgical procedures, pulmonary function studies, psychiatric evaluation, and an allergy survey.

It should be stressed that every seriously ill asthmatic patient has a medical problem and should be so treated. Studies have shown that asthmatic patients more often than not have other medical problems which may influence the asthma and which certainly must be considered in the selection of therapeutic measures for the asthma. The use of potent methods in the management of asthma presupposes an accurate appraisal of the entire patient, not merely his respiratory symptoms and especially not only the immunologic aspects of his respiratory problem. Only if the entire patient, his other diseases, his emotional problems, and the ultimate effects of therapy given him are reviewed can the best care be afforded to the asthmatic patient.

Disseminated Nodular Pulmonary Ossification with Hamman-Rich Syndrome

JOAQUIN C. VENTURA, M.D.
Montreal

LUNG NODULES consisting of bone tissue are frequently found in areas of dystrophic calcification, in sarcoidosis, in bronchiectasis, and so on, as well as in replacement of bronchial cartilage, but disseminated ossification of the lung parenchyma is rare. The first cases of the latter were published by European authors.[1,2] In 1962, Fichera and Hägerstrand[3] were able to collect only 64 cases including their own in the world literature, many of which had not been adequately documented by lung biopsy or autopsy. Reingold and Mizunoue[4] found 4 confirmed cases in the American literature, all associated with mitral stenosis, and they reported a case of idiopathic trabecular pulmonary ossification. Two types of disseminated ossification of the lung have been described, the trabecular or racemose form occurring in subjects whose average age was 64 years[5] and the far less frequent cases of nodular or tuberosa ossifications that have been observed in young people suffering from chronic stasis of the pulmonary circulation (mitral stenosis), often in association with pulmonary hemosiderosis. Small islands of lung calcification and ossification were reported by Rubin and Lubliner[6] in their review of the Hamman-Rich syndrome. The present case, diagnosed at autopsy, showed a fully developed pneumopathia osteoplastica tuberosa associated with an idiopathic diffuse interstitial pulmonary fibrosis occurring in a relatively young adult without any primary chronic heart condition.

CASE REPORT

The patient, a 40-year-old woman of French-Canadian extraction, was hospitalized from December 1961 until her death in January 1963. Eleven months before admission she had suffered from right acute pneumonia and refused hospitalization after X-ray examination. At the time, the patient's sputum was tinged with blood. After this acute episode, she continued to cough and had gray-white expectorations. Her temperature was normal, but her condition gradually deteriorated; she suffered violent headaches and progressive asthenia and perspired profusely. On admission, physical examination revealed a well-developed woman with marked signs of weight loss and dyspnea on exertion. Temperature was normal, pulse 86, respiration 30, and blood pressure 90/60. Auscultation revealed rales and fine crepitations in both lung bases. No cardiac murmur or thrill was observed. There was clubbing of the fingers. She had undergone appendectomy in 1942 and had amenorrhea at the age of 38. There was no history of exposure to dust, and the family history was not significant. X-ray examination of the lungs one month before admission to the hospital revealed numerous, disseminated, small fuzzy nodules. Her condition was diagnosed as miliary tuberculosis and probable bilateral hilar lymphadenitis with small calcified focuses. Hematologic tests revealed hemoglobin of 81% and white blood cell count of 6,000 with a differential percentage of 66 neutrophils, 4% eosinophils, 2% basophils, and 28% lymphocytes. Hematocrit was 40% and erythrocyte sedimentation rate 36 mm. The urine had a specific density of 1.012 and contained traces of albumin. On microscopic examination, a few erythrocytes and white blood cells were observed. Sputum smears and cultures for acid-fast bacilli were negative. Repeated X-ray showed fine miliary focuses distributed in both lungs. The nodules had a tendency to conglomerate and became coarser with time. The cardiac silhouette was increased in size, and the pulmonary artery was enlarged and a little fuzzy. Streptomycin, isoniazid (Rimifon®), and bed rest were prescribed, but the patient's condition progressively deteriorated and soon she developed edema of the extremities and cyanosis. In January 1963 she became unconscious and died.

JOAQUIN C. VENTURA *is with the Department of Pathology, St. Joseph of Rosemont Hospital, Montreal.*

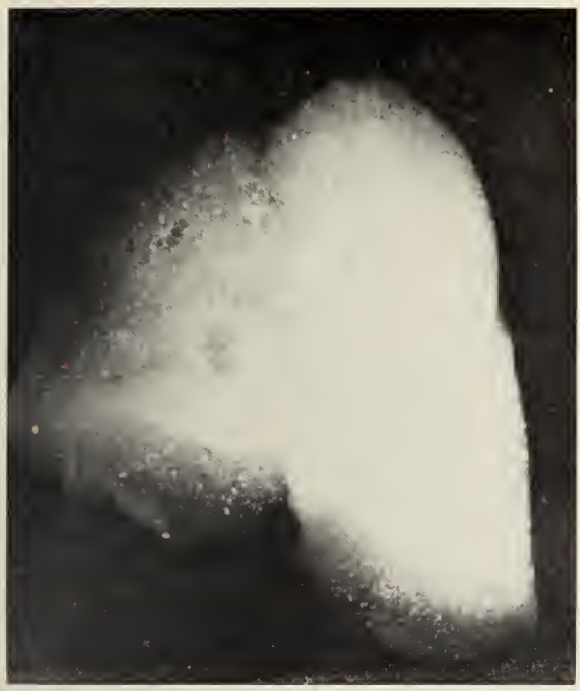

Fig. 1. Roentgenogram of the lung showing disseminated nodular opacities

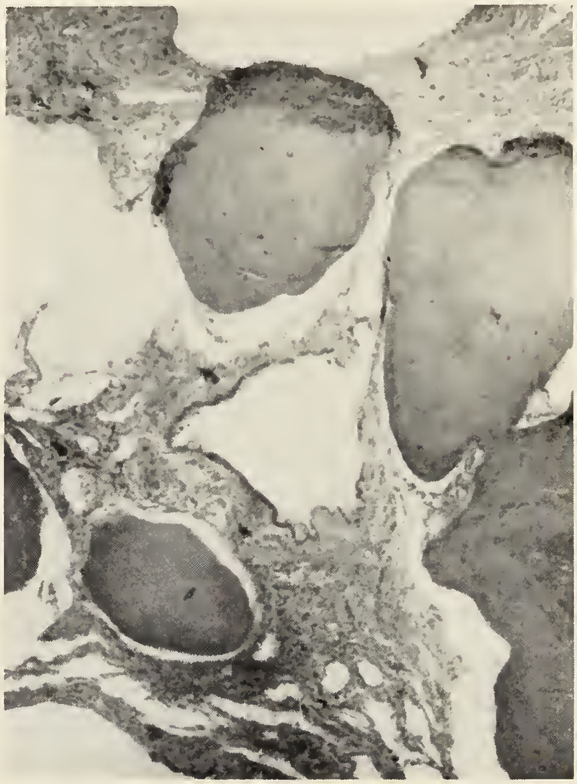

Fig. 2. Interstitial fibrosis of the lung bronchioalveolar cysts. Bone nodules lying in septa, × 38

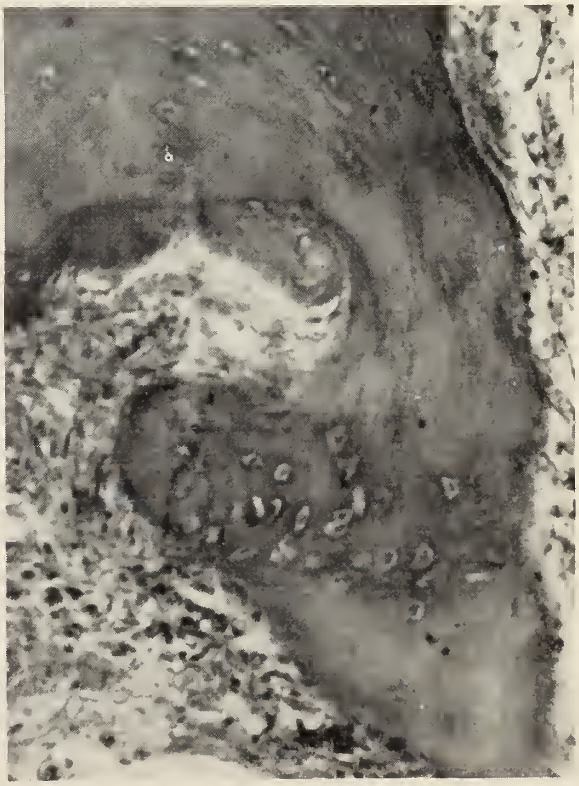

Fig. 3. Peripheral rim of osteoid in ossifying nodule, × 320

Necropsy. The legs were edematous. The lungs were contracted and weighed 800 gr. The pleural surface was shiny and presented numerous, scattered subpleural nodules measuring up to 1 mm. in diameter. The lobular pattern was indistinct with minimal anthracosis. On palpation, both lungs showed decreased crepitation and elasticity. On section, there was a grating sound and diffuse honeycombing of the organs, with innumerable small cystic spaces separated by a network of fibrous tissue. Coloration was brownish-gray, and on palpation the parenchyma resembled coarse sandpaper. Scattered throughout the lung were hundreds (Fig. 1) of small gray-white nodules measuring up to 1 mm. in size. These islands of calcified tissue were roughly round in shape and slightly more abundant near the hilar and basal segments. They were easily removed from the lung parenchyma. No calcified tissue was found in the thoracic lymph nodes. The mucous membrane of the bronchi was slightly atrophic, and small cylindrical dilations but no bronchioliths were observed. The heart was slightly enlarged with moderate hypertrophy and dilation of the right cavities. The right ventricular wall measured 0.6 cm. The valves showed no abnormal leaflets and measured as follows: tricuspid, 13 cm.; pulmonary, 9 cm.; mitral, 9 cm.; and aortic, 8 cm. Chronic congestion was observed in the liver and spleen. The thyroid and parathyroid glands appeared normal.

Histological section revealed widespread interstitial fibrosis of the lung parenchyma (Fig. 2). The fibrous tissue was diffusely infiltrated by numerous chronic inflammatory cells, and a few areas containing lymphoid follicles were seen. Entrapped dilated alveolar and terminal bronchiolar spaces were lined by hyperplastic cuboidal cells. Some of the free ends of the septa showed clubbing. Lumina contained desquamated epithelium and inspissated mucus with some neutrophils. The small and medium-sized bronchi showed hypertrophy of muscularis, hyperplasia of epithelium, and metaplasia of squamous cells. There was moderate thickening of vessel walls. No normal lung parenchyma was observed. Islands of bone were found within hypertrophic fibrous septa. Coarsely rounded nodules of mature bone contained concentric lamellae, osteocytes, calcification, and small focuses of hematopoietic marrow. Peripheral layers of bone were surrounded by a rim of osteoid (Fig. 3). No focuses of calcified tissue, other than bone, or of ossificating metaplastic cartilage were observed. Liver sections confirmed chronic passive congestions; no significant lesions were observed in the kidneys, thyroid, or parathyroid glands.

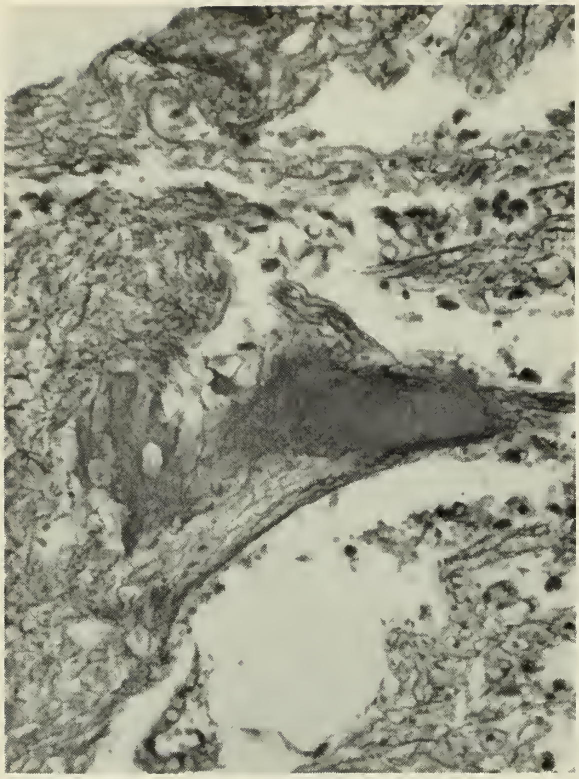

Fig. 4. Woven bone tissue in interalveolar septa, × 200

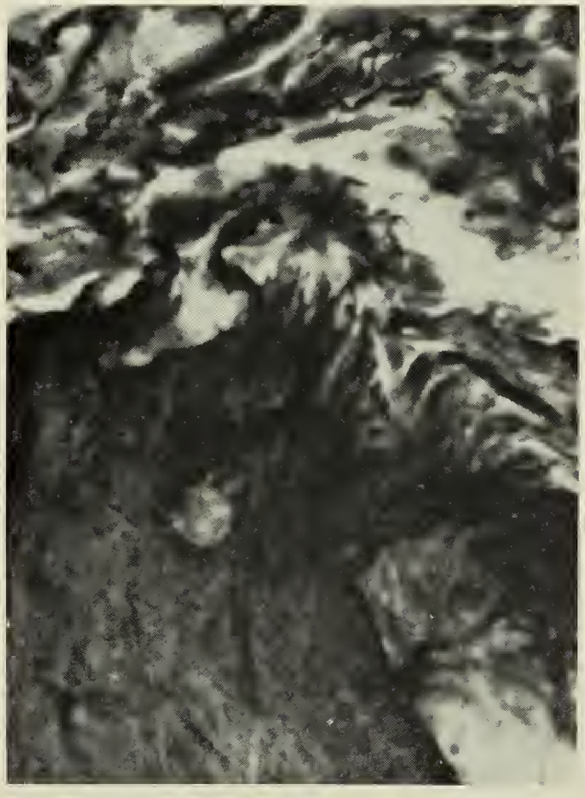

Fig. 5. Argyrophil fibers entering bone substance from intervening tissue, × 400

DISCUSSION

Disseminated and circumscribed nodular ossification of the lung parenchyma has been reported in young people, most of whom were suffering from mitral stenosis, with men under the age of 40[7] being more frequently affected than women. The development of these ossifications appeared to be closely related to the diminished blood supply to the lung and to lesions of interstitial pneumonitis.[1,8] Some authors[9] reported that the bone nodules appeared early in the onset of the rheumatic fever and before congestive failure developed. From 10 to 12 nodules in each lung ranging up to 150[3] have been reported, their size varying from 2 to 8 mm. In the present patient, islands of bone amounted to several hundreds in each lung parenchyma. The average diameter of the nodules was usually from 1 to 1.5 mm., but a few measuring up to 4 mm. were found. Although heterotopic ossification was observed underlying the visceral pleura, most frequently it was noted in the middle of thickened, fibrous, alveolar septa, as well as in close relation to periadventitious bronchiovascular tissue. Bronchioalveolar epithelium at no time was observed to be closely surrounding ossificating nodules, although inflammatory changes were sufficiently severe as to render recognition of some structures almost impossible. Inspissated mucus in cysts stained by the von Kossa method did not reveal focuses of calcification. The presence of a peripheral osteoid rim with some osteoblasts in a few nodules indicated active growth.

According to some authors,[10] ectopic metaplastic ossification may occur within a field of proliferating mesenchymal tissue, not unlike, and sometimes deriving from, reparative granulation tissue. Other factors appear to be important in the formation of ectopic bone, such as the presence of mucins, as islands of ossification are found in some epithelial and connective tissue mucin-secreting tumors. The actual inducing agent of the osteogenic response is unknown, but experimental research has shown that certain normal or devitalized tissues, such as epithelium, cartilage, and muscle, have strong bone-inductive powers. It is of interest to note the association found between the Hamman-Rich syndrome and microlithiasis alveolaris pulmonum with corpora amylacea.[11,12] Some microliths[11] showed focuses of ossification; on the basis of histochemical studies, the authors concluded that the occurrence of calcium deposition in a few corpora amylacea clearly indicates that calcification and ossification are secondary alterations in corpora amylacea. Some authors[12] feel that pulmonary concretions are the result of an inflammatory response which is probably hyperimmune to one irritant, or more likely to a variety of irritants, such as nonreabsorbed exudate, that may undergo organization and calcification and even result in disseminated ossification. In the present patient, inspissated mucus in cysts stained by the von Kossa method did not reveal focuses of calcification, and no intra-alveolar concretions were found in any part of the lung parenchyma. Ossification seemed to originate, as silver inpregnation revealed, in intraseptal focuses of condensed argyrophil fibers; these fibers were coarser than those of the intervening tissue and were characteristic of temporary woven bone (Fig. 4). Surrounding these reticulin fiber plexuses, numerous blood capillaries were noted intermingled with preosteoblasts. In more mature lamellar bone, condensation of argyrophil fibers (Fig. 5) was still observed entering bone nodules from the adjacent fibrous tissue.

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TREATMENT FOR SNAKEBITE, in addition to antivenin, antibiotics, and tetanus antitoxin, should include the light application of a tourniquet several inches proximal to the puncture. The tourniquet is loosened briefly every ten to fifteen minutes and moved to a point just ahead of the swelling. Venom can be removed with suction cups after making a small incision into subcutaneous tissue over the fang pucture. A skin test should be given before using antivenin for serious snakebite; dosage varies from 10 cc. in mild cases to 50 cc. for severe venenation. Infusions of blood, plasma, saline solution, and vasopressor drugs are required for shock. In current treatment of rattlesnake, cottonmouth moccasin, and copperhead snakebite, antihistamines and cold therapy are not recommended.

HENRY M. PARRISH, M.D., University of Missouri, Columbia. Prairie rattlesnake bites in South Dakota. S. Dak. J. Med. 18:19-24, 1965.

A Treatment for Respiratory Distress Syndrome of the Newborn

AARON FRIEDELL, M.D.
Minneapolis

THIS REPORT will present 3 cases of respiratory distress syndrome in the newborn that were helped by methods of treatment based on: (1) aiding the erection of the alveolar capillaries of the lung, and (2) removing toxic metabolites from the rectosigmoid area after the first day of life. This was done by a hot rectal wash.

The erection of the alveolar capillaries causes a distension of the alveolar space that increases the radius of the lumen of the alveoli. The increased radius makes for the practical application of LaPlace's Law, which is helpful in the treatment. The hot rectal wash removes toxic metabolites and prevents their reabsorption. It also acts as a stimulus.

Details of this method and the explanation why benefits are produced will be presented. The method of treatment was similar in all 3 cases.

TREATMENT

After resuscitation the child was examined carefully for possible congenital defects. Then treatment was instituted to include:

1. Isolette or incubator
2. Oxygen, 25 to 30%
3. Penicillin, 50,000 units intramuscularly, 4 times daily
4. The infant was held by its legs in a head-down position for twenty to thirty seconds at a time. A rest period for about a minute was allowed and the head-down position was repeated once more. Treatment was repeated every four hours.
5. The child's nostrils were compressed for five seconds. The nasal compression was released and the inspiratory effort was observed for chest expansion following the nasal compression. The infant was watched for diaphragmating (abdominal) breathing. The child was allowed to rest for a minute or two and the nasal compression was repeated 3 more times with a rest period between the nasal compressions. This was done every four hours.
6. On the day following delivery a hot rectal wash was helpful. For that purpose one-third normal saline was used at a temperature of 106° F. A plastic 30-cc. syringe was used. The hot fluid was instilled slowly with steady, mild pressure. The child was given time to expel. In a minute or two the fluid was repeated. The instillation was done 4 or 5 times a session.

If spilling was noticed when only about half the 30 cc. of fluid was instilled, the infant was allowed to expel the fluid because the rectosigmoid was contracting and expelling. The aim was to harmonize with the rectosigmoid contractions.

Respiratory distress in the newborn is a serious problem. According to Dawes,[1] 1 infant out of 300 deliveries dies of this ailment. Hence, every tangible, rational approach is deserving of trial and investigation. Respiratory distress in the newborn can be recognized. In some it starts promptly and in others it can be recognized after an hour or two. The usual findings are a rapid breathing rate above 60 or more respirations per minute with retraction of the upper abdomen and the lower chest on inspiration and with an expiratory grunt. There will be a mottled appearance of the chest X-ray. As the infant remains in distress for twenty-four to seventy-two hours and hyperventilates, gradual acidosis will set in and metabolic difficulties will accumulate.

Case 1. Born Feb. 19, 1965, firstborn of twins. Birth weight was 4 lb. 10¾ oz. The distress of this newborn was noted at once. It took nearly one hour to establish respiration. Oxygen was used for stimulation and pulmonary inflation. At the beginning the respiratory rate was 56 per minute but soon averaged 80 respirations per minute. Mild tetanic seizures were noted soon after respiration was established. Color was cyanotic. Retraction was noted in the upper abdomen and lower chest on inspiration and there was an expiratory grunt.

There was no evidence of rigidity or flaccidity. The

AARON FRIEDELL *was formerly instructor of pediatrics, University of Minnesota and is affiliated with Mt. Sinai Hospital and Methodist Hospital, Minneapolis.*

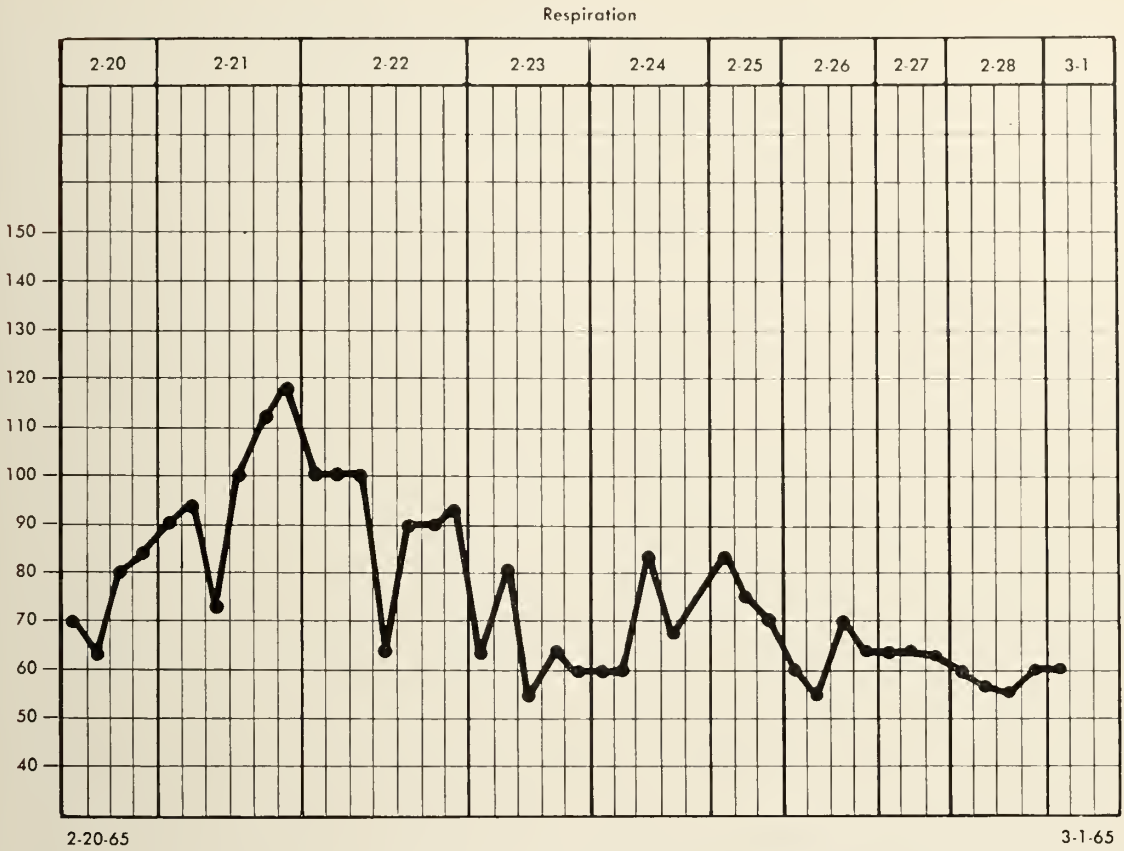

Fig. 1. Respiration chart in Case 1. Respiratory rate averaging 80 per minute was stabilized at about 60 per minute.

heart tones were of good quality. The breath sounds were rapid and shallow. The abdomen was soft; some distension was noted.

The infant's hemoglobin was 15.5 gm. The Coombs test was negative. Normoblasts numbered 76 and hematocrit was 50.

The average breathing rate of the normal newborn is somewhere between 40 and 50 respirations per minute. The respiratory rate of this infant was on the average 80 per minute (Fig. 1). At the end of the fifth day improvement was noted; the rate stabilized at about 60 respirations per minute.

This infant was in the hospital eleven days. The parents were instructed in the method of treatment and were directed how to continue the treatment at home for the following two weeks. They cooperated and the infant is doing well.

Both parents are young adults, 24 and 25 years of age. The mother had some prenatal difficulty in her last month of pregnancy. She had high blood pressure and some albumin in her urine. She was on bed rest and medication before delivery.

Case 2. A female, born Sept. 8, 1948. Birth weight was 6 lb. 8 oz. Hemoglobin was 19 gm. The respiratory rate averaged 56 per minute. Respiratory distress was noted the following day. Diagnosis was established by X-ray as severe atelectasis.

The mother was 34 years old. She was hypertensive during her last trimester and had a 1+ albumin in her urine.

This infant was treated by nasal compression and the hot rectal wash. She was kept at rest in a head-down, inclined position of about 30°.

The baby was discharged on Sept. 20, 1948. Length of her hospital stay was twelve days.

Case 3. A male, born July 9, 1954, two weeks premature. Birth weight was 5 lb. Hemoglobin was 20 gm. Respiratory rate averaged between 50 and 60 per minute.

Distress was noted on the second day of life. His color was poor. There was retraction of the abdomen and the lower chest on inspiration and occasional grunting with expiration. The method of treatment was similar to that of case 1.

The child was discharged from the hospital on July 21, 1954. Length of his hospital stay was 12 days.

DISCUSSION

The objective in this treatment of keeping the infant in the head-down position and compressing the nose is to improve the erection of the alveolar capillaries.

The erection of the alveolar capillaries plays an important part in life. According to Redbard,[2] the alveolar capillaries distend and enlarge to some extent with every inhalation (Fig. 2) and return to the original volume with exhala-

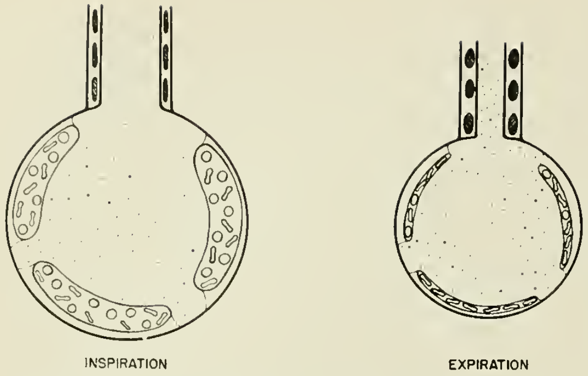

Fig. 2. Schema to illustrate the effect of respiration on the pulmonary circulation. The alveolus in inspiration is shown with large volume. Its contained air is indicated by the widely separated dots representing relative rarefaction due to the diminished intra-alveolar pressure. The bronchiole is widely dilated, permitting free access of air into the alveolar chamber. The reduced intra-alveolar pressure permits engorgement of the pulmonary capillaries shown filled with red blood cells. The alveolus in expiration is smaller due to the diminished air volume. The bronchiole is constricted, increasing the resistance to outflow of air. The increased air pressure in the alveolus, suggested by the greater concentration of dots, acts to compress the capillaries and thus increases the resistance to flow through these vessels. (S. Rodbard. Bronchomotor Tone. Amer. J. Med. 15:356, 1953.)

tion.[3] When the infant is held briefly by his legs in a head-down position there will be a momentary increase in the pulmonary artery pressure. This is because both the pulmonary artery and the cystic duct (lymph flow) will be aided by gravity to increase the flow and pressure to the pulmonary artery and the alveolar capillaries.

It may be advantageous to recall that the pulmonary artery delivers its blood flow directly to the terminal arterioles and the alveolar capillaries. When the body is held in a head-down position the force of gravity is more favorable to both the venous and lymph flow as they both deliver directly to terminal arterioles which improves the erection of the alveolar capillaries.

Carter and Bonham[4] and Jaykka[5] called attention to the importance of the alveolar erectile capillaries. "The pulmonary capillaries are erectile and help to hold out alveoli as a result of their distending with blood. The high venous pressure, measured in the anterior vena cava, is beneficial to premature neonates with respiratory difficulty shortly after birth. This benefit is derived from a high cardiac output (stroke volume) dependent on the high venous pressure. Where the peripheral pulmonary vascular resistance is very high, probably due to asphyxia, a high cardiac output is necessary to overcome it, so that the pulmonary capillaries may be adequately filled with blood and play their part in the proper extension of the alveoli.

"The rigidity and the flaccidity of the capillary network, the property which is most responsible for this, will be the tension in the wall of the capillary. This tension, as in a tire, will be related not only to the pressure within the tube, but also to the radius and diameter of the tube."

Holding the infant in the head-down position should increase the cardiac output. This is the application of LaPlace's Law: "The tension in the wall of the cylinder is equal to the distending pressure multiplied by the radius." Distension of the terminal arterioles, the alveoli, and the alveolar capillaries enlarges the alveolar space making more red blood cells and more oxygen available. Thus, the increased pressure will improve the pulmonary function and oxygenation. Wm. F. Windle and co-workers[6] corroborate this attitude. "If air or oxygen is introduced by attempts of artificial respiration then the proximal air spaces and those in localized portions in certain lobules will become hyperdistended. Globular spaces are then produced which can usually be identified on microscopic examination as being the result of this procedure. But when fluid is introduced into the alveolar capillaries, then things are different." The pulmonary artery can fill and distend all the capillaries and the alveoli. Artificial respiration does not do as well.

The blood flow as influenced by respiration does not open up all of the alveolar capillaries. Some capillaries remain closed. But by the reversal of posture to a head-down position for a few seconds the capillaries are exposed to the pulmonary artery pressure and all the capillaries function temporarily.

The lungs receive blood from 2 separate sources: one from the arterial blood through the bronchial arteries that supplies nutrition to all of the lung tissues, and second from the pulmonary artery that delivers venous blood directly to the terminal arterioles and alveoli for gaseous exchange. Holding the infant briefly by his feet in a head-down position will favor the delivery of more blood to the alveolar capillaries and will make them erectile.

COMPRESSION OF THE NOSTRILS

The second step is to compress the nostrils of the infant for five seconds at a time. A newborn child does not breath through his mouth. At birth, if the child's nostrils are compressed, he cannot breathe for a few seconds. Normally the respiratory rate of the newborn will be about 40 to 50 per minute. If distressed the infant breathes at a much higher rate and goes into hyperventilation. The highest rate of case 1 was 90 to 120 per minute.

With rapid respiration the infant does not get enough oxygen deep into the alveoli. As a matter of fact, he does not quite expire enough carbon dioxide. The child is in hyperventilation and yet has increased carbon dioxide retained due to shallow expiration. Undoubtedly, the infant goes into metabolic acidosis because he does not exhale enough carbon dioxide. Apparently the alveoli do not function adequately. They do not fill up with air nor do they empty completely. When the nostrils were held for five seconds we temporarily reduced the respiratory rate to 12 per minute. Carbon dioxide continued to reach the alveoli. When the nostrils were released we noticed that the child gasped for breath once or twice. In other words, he inhaled forcefully a little more into his own alveoli during the few moments of struggle and apparently also exhaled more efficiently. By so doing he inhaled and exhaled more forcefully and increased his intrapulmonary pressure.

Hence, the baby's nostrils should be compressed for five seconds and released promptly to see if he distends the lower chest on inhalation and has diaphragmatic breathing. This should be repeated 4 or 5 times a session, 5 times a day.

Many researchers[7,8] have observed that air pressure at 25 cm. of water are necessary to distend the lungs of a newborn infant. Even a water pressure of 25 cm. when forced in resuscitation may injure lung tissue. Smith and Chisholm[7] pointed out "that the struggling infant can safely increase its own inflating pressure to 40 cm. of water pressure without injury but the distending pressure of only 25 mm. water pressure used on resuscitation may injure the lungs by overdistension." Better results can be obtained by brief nasal compression.

When the child inhales deeply, the lower chest and abdomen, and then the alveoli, terminal arterioles, and bronchi are distended. Also nerve endings of the vagus nerve supplying the lungs are distended and stretched.

W. B. Cannon of Harvard University,[9] called attention to the fact that the sympathetic nervous system gives off sympathin or adrenalin and the parasympathetic will give off acetylcholine which, in turn, produces vasodilation.

On deep inhalation the infant distends the terminal bronchioles and alveoli. He stretches and stimulates mechanically the terminal endings of the vagus nerve and thereby receives benefit.

That was corroborated by Geofry Dawes[1] who observed that if he injected acetylcholine it caused pulmonary vasodilation so that the blood flow increased sixfold.

Similarly, Miller and associates[8] concluded that "respiration patterns in newborn infants as determined by air flow and pneumographic studies have their possible relationship to a deficient vagal mechanics." In that article they stated: "In a recent study it was shown hyaline membrane in the lungs of rabbits were similar in appearance, distribution, and histochemical construction to those occurring in the lungs of a newborn infant. There was similarity in vagotomized rabbits and in infants dying of hyaline membrane disease. These observations raised the question as to whether or not pulmonary symptoms in dying newborn infants were also the result of a deficient vagal control of respiration. Rapid respirations up to 104 per minute have been observed before death." They believe "inability to develop diaphragmatic contractions may be an important factor in the neonatal death that occurs in the first few days of life. A poorly developed vagal mechanism may be one of the factors causing inadequate diaphragmatic activity."

Coombs and Pike[10] made a comprehensive survey of the mechanism in control of respiration in kittens from birth to sixty-three days old. "The vagus control over the movements of the diaphragm appears to be acquired earlier than regulation of any other portion of the afferent system. It would appear that at birth the respiratory mechanism is a relatively simple pathway in which the vagi and phrenics are the chief afferent and efferent nerves of the respiratory center."

Since structure influences function and function influences structure, it would appear then that when we distend the terminal lung structures, the bronchioles, and the alveoli, we also distend the terminal nerve endings of the vagus. In other words, when we turn the infant upside down for a few seconds and cause a distension of the pulmonary artery, the terminal arterioles, and the alveoli, we also cause a stretching and a mechanical stimulation of the nerve endings of the vagus, for vagal nerve endings are in close contact with the terminal structures of the lung.

We also accomplish the same objective by holding the infant's nostrils for a few seconds to compel him to breathe deeply following the nasal compression. Deeper breaths distend the terminal bronchi and also stretch the vagus nerve endings.

Boyd[11] noticed that "specialized pressor-receptor nerve endings are found in arteries of the adult mammal which are persistent portions of the embryonic bronchial arch arterial pattern." He quotes Takino and Watanaba who described the slowing of the heart and a marked fall in blood pressure following mechanical or electrical stimulation of the pulmonary artery. I conclude that keeping the infant in the inverse posture and brief nasal compression are of help.

THE HOT RECTAL WASH

The object of doing a hot rectal wash, beginning on the second day of life in the infant in distress, is twofold:

1. It aids in the elimination of toxic metabolites from the rectosigmoid area where metabolites may be reabsorbed and act as a toxic feedback to the infant.

2. It is an effective general body stimulant.[12–16]

SUMMARY

Keeping the infant in the head-down position for a few seconds allows the pulmonary artery to fill the terminal arteries and alveolar capillaries and to become erectile. Similar benefits are obtained by compression of the child's nostrils for five seconds, to compel the infant to take a deep breath following the nasal compression.

When the terminal arterioles and capillaries become erectile, they enlarge and distend the alveoli and stretch the terminal nerve endings of the vagi. Most likely, endogenous production of acetylcholine takes place to enhance the blood flow.

In distending the terminal bronchioles and alveoli, LaPlace's Law is applied that apparently helps to improve the circulation and oxidation. The hot rectal wash is used to improve elimination and body stimulation.

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INTRA-ABDOMINAL HEMORRAGE or visceral injury may exist in blunt injuries of the pelvis, abdomen, or chest. Use of a modified technique of diagnostic peritoneal lavage sharply reduces the high mortality rate that otherwise results when these conditions are undetected. The entire abdominal cavity is monitored through one puncture site and indications for laparotomy are prompt and infallible. The technique, which also identifies intra-abdominal conditions not associated with physical trauma, is especially useful in comatose patients with confusing clinical signs and where risk of exploratory laparotomy is formidable.

HARLAN D. ROOT, M.D., CHARLES W. HAUSER, M.D., C. RICHARD MC KINLEY, M.D., JAMES W. LA FAVE, M.D., and RAMON P. MENDIOLA, JR., M.D., Ancker Hospital, St. Paul, and University of Minnesota, Minneapolis. Diagnostic peritoneal lavage. Surgery 57:633-637, 1965.

Use of Oral Iron in Anemia Associated with Gastrointestinal Disorders

PHILIP R. NAST, M.D., and JAMES L. A. ROTH, M.D.
Philadelphia

IT IS WIDELY KNOWN that many of the iron salts now in use in the oral treatment of iron-deficiency anemias may cause unpleasant side reactions, which may restrict or hinder adequate therapy. It is our experience that these reactions particularly occur in the treatment of anemia secondary to hemorrhage from a gastrointestinal lesion.

Such unpleasant reactions as nausea, vomiting, abdominal colic, constipation, pyrosis, and even diarrhea have been reported in as high as one-third of the patients treated.[1-3] These side effects are usually proportional to the size of the dose. If one persists in ordering such doses of a poorly tolerated iron preparation, the patient often abandons therapy.

The unpleasant side reactions are the results of the large amount of nonabsorbed elemental iron remaining in the gastrointestinal tract. The ferrous iron is absorbed chiefly in the duodenal region, but apparently the rest of the gastrointestinal tract has the capacity to absorb iron if the iron is still in the ferrous form.[4] At acid pH certain substances in the food serve to reduce the ferric forms to the ferrous forms. When achlorhydria is produced by gastric resection or when the major site of absorption in the duodenum is removed by a gastroenterostomy, a hypochromic anemia due to iron deficiency may develop.[5]

Another problem exists in the treatment of anemias with oral iron in patients who have lesions in the gastrointestinal tract. The administration of preparations containing a large amount of iron produces a black-colored stool resembling the tarry stool of melena and may thus obscure this valuable clinical sign of gastrointestinal bleeding. In some cases this may even produce a false-positive reaction for occult blood.[4]

In recent years Ausman[6,7] has reported the effectiveness of ferrous gluconate-polyoxyethylene glucitan sorbitan monolaurate combination (Simron®) in patients with iron-deficiency anemia. Simron® was highly effective in raising the hemoglobin level and the percentage utilization of iron and was well tolerated, well absorbed, and relatively free from side effects. Ausman's studies showed that absorption and utilization were indeed better with Simron® than with ferrous sulfate, a ferroglycine sulfate complex, or a ferrous sulfate and cobalt preparation in those patients who had received previous courses of iron therapy. Some of the patients reported had lesions of the gastrointestinal tract.

The purpose of the study reported here was to determine the effectiveness and tolerance of Simron® in patients with iron-deficiency anemia who had lesions in the gastrointestinal tract.

METHODS AND MATERIALS

Patients. The patients studied were chosen from the private practices of the authors and the wards and clinics of the gastroenterology services of the Bryn Mawr Hospital and the Graduate Hospital of the University of Pennsylvania. The patients selected had primary gastrointestinal diagnoses and an iron-deficiency–type anemia.

Ages of the 49 patients (27 males, 22 females) ranged from 18 to 87 years. Nine patients did not complete the study due to death, surgical intervention, or lack of cooperation.

The patients were divided into 2 main groups. Group A was composed of 31 patients with primary disorders of the esophagus, stomach, or duodenum. Group B, numbering 18, included patients with primary disorders of the small bowel and colon. The diagnosis in each patient was well established by X-ray, gastroscopy, small bowel biopsy, sigmoidoscopy, or other methods deemed

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PHILIP R. NAST *is with the Bryn Mawr Hospital, Bryn Mawr, Pennsylvania.*

JAMES L. A. ROTH *is director, Division of Gastroenterology, the Graduate School of Medicine, University of Pennsylvania, Philadelphia.*

necessary. All patients with acute massive gastrointestinal bleeding were allowed to stabilize before Simron® therapy was instituted. If any transfusions were required in the management of these patients, the initial laboratory values in this study represent those values obtained after the patient had stabilized and required no further blood transfusions.

Dosage. The dosage of Simron® was arbitrarily selected. Three, 4, 6, or 8 capsules per day in 3 or 4 divided doses were used with the higher dosage being used in the more severe anemias. The duration of therapy lasted from two to twenty-six weeks, except for 1 patient who was hypersensitive to the drug, and treatment was terminated after one day.

Evaluations. The pretreatment evaluations included hemoglobin, hematocrit, red blood count, and reticulocyte count. Hospitalized patients were checked daily for side reactions and hematologically twice a week. Those treated as outpatients were checked at least every two weeks for side reactions and hematologic response. The reticulocyte count was checked twice a week until the maximum response was noted. The final evaluation included the same hematologic studies.

Twenty-six of the 49 patients also had detailed iron studies and hematologic indexes initially. The course of therapy was sufficiently uninterrupted in 13 of these 26 patients to permit similar detailed iron and hematologic studies after treatment. Bone marrow studies were obtained on 10 of these 13 patients. A gastric analysis was performed in 24 patients in Group A; either Ewald test meal, histamine, or caffeine was used as a stimulus.

The side effects particularly looked for included nausea, vomiting, diarrhea, constipation, abdominal colic, pyrosis, anorexia, and melena.

RESULTS

Group A (31 patients). The results in patients with primary gastrointestinal lesions involving the esophagus, stomach, or duodenum are summarized in table 1. Over 50% of these patients had frank peptic ulcer disease with acute hemorrhage and were hospitalized. Thirteen patients required blood transfusions during the ten to fourteen days before Simron® therapy was instituted. In 7 patients the results were considered invalid because the patient either died, was transfused with blood during Simron® therapy, or did not return sufficiently often for adequate evaluation. A good hematologic response was obtained in 23 of the remaining 24 patients. The one patient who had no response (case 18) was a 70-year-old male treated for six weeks with 6 Simron® capsules per day. This patient had iron-deficiency anemia for many years following a subtotal gastrectomy in 1950. He had failed previously to respond to oral iron of other types on many occasions. However, he did respond to parenteral iron. Detailed radioactive oral iron uptake studies were performed and showed that he absorbed little if any of the iron preparation given to him by mouth. In addition, his iron-binding capacity was 437 μg. per 100 ml. His bone marrow was very cellular. He died of acute myocardial infarction six weeks after the study was started.

The response to Simron® was slower than desired in patient 31. However, this 43-year-old female cooperated poorly and it is estimated that her average dose of Simron® over the thirteen weeks of therapy was only 1 capsule a day instead of the 4 as ordered.

Patients 20, 29, and 30 are most interesting in that studies showed they had a severe iron-deficiency anemia and 2 had no free acid after a histamine gastric analysis. All 3 patients had had subtotal gastrectomies with a Billroth II anastomosis. A good response to therapy was obtained in all 3, although the duration of therapy was longer than average. Four other patients (6, 12, 17, 21) with achlorhydria also had a good response.

Group B (18 patients). The results in patients with primary gastrointestinal lesions involving the small bowel or colon are summarized in table 2. Twelve of these 18 patients had either ulcerative colitis, ileocolitis, or regional enteritis. Data for 2 patients in this group (34 and 36) were inadequate. Patient 34 required transfusions and surgical management of fulminating disease after two weeks of treatment. Patient 36 was very ill with ulcerative colitis; her intolerance of the drug will be discussed later.

This group of patients presented a different problem in that they had chronic continuous blood loss and active disease when therapy was instituted. Many of them required other forms of simultaneous management (Table 2). Fourteen of the remaining 16 patients had a good response. Patient 32 did not respond to oral therapy after eleven weeks. Studies revealed a malabsorption syndrome with absent small bowel villi and postoperative steatorrhea following a bowel resection for intussusception. The subsequent good response to parenteral iron was in keeping with the underlying malabsorption problem. An increase of only 1 gm. per 100 ml. of hemoglobin was obtained in patient 40 after six weeks.

Detailed hematologic studies. Twelve of the 13 patients studied in detail before, during, and

TABLE 1

HEMOGLOBIN RESPONSE OF PATIENTS IN GROUP A

Patient No.	Patient Age	Patient Sex	Diagnosis	Dosage (capsules of Simron®)	Duration of therapy (weeks)	Hemoglobin (grams per 100 ml.) Initial	Final	Change	Maximum gastric acid (free/total)	Comment
1	75	M	Peptic esophagitis	1 Q.I.D.	7	8.2	13.3	+5.1	101/108 units	
2	68	M	Hiatus hernia	1 Q.I.D.	4	9.3	13.8	+4.5	59/ 76 units	
3	66	M	Esophagus varices	1 Q.I.D.	7	10.9	14.6	+3.7		
4	55	F	Hiatus hernia	1 Q.I.D.	9	11.2	14.5	+3.3		
5	40	M	Pyloric ulcer	1 Q.I.D.	6	11.2	14.9	+3.7	22/ 41 units	
6	55	F	Erosive gastritis	2 Q.I.D.	9	9.4	14.4	+5.0	0/ 29 units	
7	49	M	Gastric ulcer	2 T.I.D.	9	10.4	15.5	+5.1	51/ 75 units	
8	87	F	Malignant gastric ulcer	1 Q.I.D.	1	11.3	—	—		Died[°]
9	74	F	Pyloric ulcer	2 Q.I.D.		6.8	—	—		Did not return[°]
10	81	M	Gastric ulcer	2 Q.I.D.		5.0	—	—	50/ 68 units	Transfused[°]
11	35	F	Gastric ulcer	2 Q.I.D.	16	8.5	13.7	+5.2	54/ 66 units	
12	69	M	Marginal ulcer	1 Q.I.D.	14	10.5	14.0	+3.5	achlorhydric	
13	50	F	Salicylate erosions	1 Q.I.D.	11	9.5	14.3	+4.8	40/ ? units	
14	34	M	Duodenal ulcer	2 Q.I.D.	7	7.4	15.5	+8.1	53/ 71 units	
15	84	F	Duodenal ulcer	2 T.I.D.	4	11.2	12.8	+1.6	28/ 38 units	
16	43	M	Postgastrectomy anemia	2 Q.I.D.	5	8.5	9.7	+1.2	0/ 29 units	Did not return[°]
17	50	M	Gastric varices	2 Q.I.D.	4	5.8	10.5	+4.7	0/ 18 units	
18	70	M	Postgastrectomy anemia	2 T.I.D.	6	10.6	10.5	−0.1	0/ 20 units	Died, infarction
19	37	M	Duodenal ulcer	2 T.I.D.	13	11.3	13.9	+2.6	26/ 42 units	
20	65	F	Postgastrectomy anemia	2 Q.I.D.	26	7.0	13.7	+6.7	18/ 36 units	
21	44	F	Erosive gastritis	2 Q.I.D.	10	5.9	13.7	+7.8	0/ 10 units	
22	64	F	Duodenal ulcer	2 Q.I.D.	11	9.2	13.9	+4.7	10/ 45 units	
23	70	M	Duodenal ulcer	2 Q.I.D.		8.6	—	—		Did not return[°]
24	70	F	Salicylate erosions	2 T.I.D.	2	9.9	12.2	+2.3		
25	68	M	Marginal ulcer	1 T.I.D.	2	8.1	9.5	+1.4	43/ 70 units	Died[°]
26	18	M	Duodenal ulcer	1 T.I.D.	4	10.8	15.0	+4.2	47/ 60 units	
27	53	M	Duodenal ulcer	2 Q.I.D.	2	8.3	—	—		Gastrectomy hemorrhage[°]
28	74	M	Duodenal ulcer	2 T.I.D.	9	9.8	16.1	+6.3	95/120 units	
29	47	F	Postgastrectomy anemia	2 Q.I.D.	21	7.0	12.8	+5.8	0/ 23 units	
30	48	F	Duodenal ulcer, postgastrectomy	1 Q.I.D.	20	9.2	13.3	+4.1	achlorhydric after gastrectomy hemorrhage	Rx started after gastrectomy hemorrhage
31	43	F	Duodenal ulcer	1 Q.I.D.	13	10.9	12.7	+1.8	60/ ? units	

[°] Inadequate studies

TABLE 2

HEMOGLOBIN RESPONSE OF PATIENTS IN GROUP B

Patient						*Hemoglobin (grams per 100 ml.)*			
No.	*Age*	*Sex*	*Diagnosis*	*Dosage (capsules of Simron®)*	*Duration of therapy (weeks)*	*Initial*	*Final*	*Change*	*Comment*
32	34	F	Intussusception, malabsorption, resection	1 Q.I.D.	11	10.9	10.2	−0.7	Prednisone also
33	57	M	Regional enteritis	1 Q.I.D.	17	10.2	13.1	+2.9	Azulfidine also
34	23	M	Ileocolitis	2 Q.I.D.	2	9.7	10.4	+0.7	Transfused and ileostomy after two weeks' therapy*
35	20	M	Ileocolitis	1 Q.I.D.	16	10.4	15.0	+4.6	Ileotransverse colostomy at onset of study
36	54	F	Ulcerative colitis	1 capsule	1 day	9.5	—	—	Could not tolerate*
37	83	F	Diverticulitis	2 T.I.D.	3	10.3	13.0	+2.7	
38	69	M	Cancer of left colon	1 T.I.D.	4	11.5	14.2	+2.7	Colectomy after study
39	70	F	Melanosis coli with hemorrhage	2 T.I.D.	13	9.4	14.1	+4.7	
40	51	F	Irritable colon with menorrhagia	1 T.I.D.	6	11.2	12.2	+1.0	
41	61	F	Colonic polyp	1 T.I.D.	16	11.5	14.4	+2.9	Length of therapy approximate
42	21	M	Ulcerative colitis	1 Q.I.D.	12	11.4	15.2	+3.8	Azulfidine also
43	58	M	Ulcerative colitis	1 Q.I.D.	9	10.7	15.3	+4.6	Azulfidine and prednisone also
44	24	F	Ulcerative colitis	1 Q.I.D.	6	10.0	14.0	+4.0	Azulfidine also
45	51	M	Ulcerative colitis	1 Q.I.D.	10	9.5	14.0	+4.5	Azulfidine also
46	27	M	Ulcerative colitis	1 T.I.D.	10	10.5	13.7	+3.2	
47	22	F	Ulcerative colitis	1 Q.I.D.	13	9.8	13.0	+3.2	Prednisone also
48	20	M	Ulcerative colitis	1 Q.I.D.	11	10.7	13.5	+2.8	Azulfidine also
49	27	M	Ulcerative colitis	1 Q.I.D.	10	9.1	14.8	+5.7	Prednisone also

*Inadequate studies

after treatment were in group A and 1 was in group B. Table 3 summarizes these studies. It can be noted that the lowest abnormal indexes were found in the chronic bleeders. Except for patient 1, the highest iron-binding capacity levels were obtained in the chronic anemias. This is in keeping with the expected results in severe iron-deficiency–type anemias. In all patients with chronic blood loss, the final serum iron levels were well elevated into the normal range, whereas, in the acute bleeding patients this was not so. This might mean we did not continue the therapy long enough in these acute cases to replenish the iron stores.

Patient 14 was an exception to the above general observation in patients with acute bleeding. Massive hemorrhage complicated duodenal ulcer disease in this patient and required 7 units of whole blood to stabilize hemodynamics ten days before the study. This patient had an initial low serum iron that returned to normal after treatment. This patient will be discussed further with respect to special iron studies on the bone marrow.

The reticulocyte responses were erratic and may represent poor timing in obtaining them. All bone marrows before treatment showed marked or moderate erythroid hyperplasia. In most patients with acute hemorrhage, no microcytosis or hypochromia was noted. In the chronic bleeding patients, the anticipated hypochromia and microcytosis of the red cells in the marrow were noted.

SIDE EFFECTS

The tolerance to Simron® was excellent. Only in patient 36 did we encounter any serious complaint. This patient had severe fulminating ulcerative colitis. Within eight hours after administrating the first capsules of Simron®, she complained of severe rectal burning. A second trial of only one capsule resulted in the same intolerable reaction within six hours. A third trial was given to this patient when the contents of the capsule were added to the food without her knowledge and the same rectal burning occurred. No other patient had a similar side effect.

Mild constipation was reported by 4 patients. Three of the 4 were taking 8 capsules of Simron® per day. With reduction of the dose to 6 capsules per day for only forty-eight hours, the constipation subsided and resumption of 8 capsules per day did not result in a recurrence. In general when this complaint was elicited in these 4 patients, constipation was so minimal that the patients mentioned it only on direct questioning. By contrast, patients 1 and 15 were started on Simron® because of previous intolerable constipation while on ferrous sulfate and subsequently developed no side effects.

Four patients, one of whom also had constipation, reported a color change in the stool occurring periodically during treatment. The color was not black or tarry as in melena, but a definite greenish or greenish-brown color. This was usually noted for only short intervals of one to three days on several occasions during treatment. The stools were tested frequently for occult blood by several methods, such as guaiac, benzidine, Hematest, and Gregerson. Nausea, vomiting, colic, or pyrosis was not experienced by the patients in this study.

DISCUSSION

The most direct method of assessing the iron stores is the examination of fragments of sternal bone marrow for stainable iron. The percentage of stainable iron-containing normoblasts (sideroblasts) in smears of bone marrow can be used as a reliable means of detecting iron deficiency.[8] When the hemoglobin is higher than 9 gm. per 100 ml. the serum iron and iron-binding capacity are a much less reliable index of iron depletion. Also, in this group characteristic hypochromia and microcytosis are often absent, as we found in our acute bleeding patients (Table 3).

The use of the Prussian blue reaction for hemosiderin in bone marrow particles and normoblasts was first introduced in 1948.[9] This reaction has been useful diagnostically in distinguishing iron-deficiency anemia from other microcytic, hypochromic anemias with low serum iron values; in distinguishing concomitant iron deficiency in a patient with anemia produced by another condition; and in studying iron deficiency in a patient who for some reason does not respond to oral iron, such as patient 18.[10]

We used this technique to search for iron in the sternal bone marrows obtained before treatment. In no patient did we find evidence of stainable iron-containing normoblasts, suggesting depleted iron stores. Two patients were selected for a second evaluation after treatment was completed. Patient 29 (postgastrectomy anemia) had her second sternal marrow study after twenty-one weeks of Simron® when her hemoglobin was 12.8 gm. per 100 ml. This marrow, however, did not have any stainable iron-containing normoblasts and the smear still revealed mild hypochromia. Interestingly, a short time after discontinuing Simron®, this patient's hemoglobin dropped to 8.5 gm. per 100 ml. and again responded to Simron® therapy. Simron® is now being continued for an extended period of time

TABLE 3

RESPONSE OF 13 PATIENTS STUDIED IN DETAIL

No. Pt.	*Hemoglobin (grams per 100 ml.)*		*HCT (percent)*		*RBC (millions)*		*MCH (µg.)*		*MCV (cu. µ)*		*MCHC percent*		*Maximum retic. response (percent)*	*Serum iron (µg. per 100 ml.)*		*Iron-binding capacity (µg. per 100 ml.)*		*Bone marrow study*	*Blood loss*
	I.	*F.*	*I.*	*F.*	*I.*	*F.*	*I.*	*F.*	*I.*	*F.*	*I.*	*F.*		*I.*	*F.*	*I.*	*F.*		
1	8.2	13.3	30.4	40.5	3.67		22		84		27		1.1	37	111	142	231	+	Chronic
5	11.2	14.9	34.4	47.5	4.27	5.28	27.4	29	90.8	92	30.1	32	0.7	54	40	357	416	+	Acute
6	9.4	14.4	28.1	43.7	3.12	4.48	30	31	91.5	93.5	33.5	33.5	6.8	46	49	322	394	+	Acute
7	10.4	15.5	31	45.5	3.45	5.30	30	29	90	86	34	34.5	2.9	40	54	297	350	+	Acute
11	8.5	13.7	31.3	42	4.12	4.20	20	30.5	77	92	27	33.5	1.5	17	80	399	341		Chronic
14	7.4	15.5	24	46.8	2.52	5.38	29	29	96	88	31	33.5	8.8	31	80	294	379	++	Acute
15	11.2	12.8	34.4	41.1	3.80		29.2		91		32.5		3.1	29	23	277	265	+	Acute
19	11.3	13.9	35.5	41.3	3.57	4.22	34	32	98	96	35	33	1.3	71	95	379	388	+	Acute
20	7.0	13.7	23.5	36.1	3.76	4.24	19	28.5	63	87	30	33.5	1.4	8	49	486	365	+	Chronic
21	5.9	13.7	24		3.66	4.10	16	29	66	96	25	32	3.0	17	63	387	362	+	Chronic
28	9.8	16.1	29.5	43.4	3.30	4.95	29	33	89	89	34	35	2.0	34	43	336	357		Acute
29	7.0	12.8	26.4	41.2	4.12	5.00	17	25.5	64	83	27	31.5	2.1	14	151	421	455	++	Chronic
39	9.4	14.1	27.6		2.86	4.40	33		99		34		5.0	31	43	329	353		Acute

I=Initial
F=Final
HCT=Hematocrit
RBC=Red blood count
MCH=Mean corpuscular hemoglobin. Normal range: 28-32

MCV=Mean corpuscular volume. Normal range: 83.5-94.5
MCHC=Mean corpuscular hemoglobin concentration. Normal range: 32-34
+=Bone marrow study was performed.
Serum iron, normal range: male 53-154 µg. per 100 ml.; female 58-145 µg. per 100 ml.
Iron-binding capacity, normal range: male 257-413 µg. per 100 ml.; female 298-433 µg. per 100 ml.

because of the lack of stainable iron in the marrow in spite of the high serum iron level. Patient 14 also had no detectable iron in the bone marrow before treatment. After seven weeks of Simron® therapy, when the hemoglobin and the serum iron were both normal, the repeat bone marrow study showed iron-containing normoblasts.

SUMMARY

The hematinic product, ferrous gluconate-polyoxyethylene sorbitan monolaurate combination (Simron®), is a convenient and effective oral iron preparation for the treatment of iron-deficiency anemia. Simron® is well tolerated by patients with lesions of the gastrointestinal tract, including peptic esophagitis, hiatus hernia, esophageal varices, gastric ulcer, erosive gastritis, duodenal ulcer, postgastrectomy anemia, marginal ulcer, regional enteritis, ileocolitis, ulcerative colitis, and diverticulitis. Simron® did not cause melena to obscure a valuable clinical sign of gastrointestinal bleeding in this study. The value of iron stains for hemosiderin in bone marrow smears has been emphasized.

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METASTASIS of rectal carcinoid tumors is determined by size rather than cellular characteristics. Deep invasion or metastasis is unlikely if the lesion is less than 1 cm. in diameter, and fulguration seems to be as satisfactory as local excision. Approximately half of tumors 1 to 2 cm. in diameter are more aggressive. Local excision provides a more adequate specimen for histological study, and radical surgical excision is indicated if muscular invasion is evident and if tumors are larger than 2 cm.

VINCENT T. CALDAROLA, M.D., RAYMOND J. JACKMAN, M.D., CHARLES G. MOERTEL, M.D., and MALCOLM B. DOCKERTY, M.D., Mayo Clinic and Foundation, Rochester, Minn. Carcinoid tumors of the rectum. Amer. J. Surg. 107:844-849, 1964.

A HIGH CURE RATE may be expected with prompt diagnosis of carcinoma originating in the glottis. Most significant early warning is persistent hoarseness. Respiratory difficulties and secretions causing periodic clearing of the throat may occur later. Abnormal swelling or ulceration of vocal cord, determined by laryngeal mirror examinations, calls for definitive diagnosis by direct laryngoscopic and biopsy techniques. Although malignant growth is slow at first, metastatic spread is rapid once the lesion extends beyond the glottis. Treatment may be irradiation, cord excision, total laryngectomy, or monoblock laryngectomy with radical neck dissection, depending on extent of malignancy. All glottic lesions in 108 patients were squamous-cell carcinomas. With early diagnosis 35 of 39 patients survived four and half to nine years after treatment.

JOHN R. HILGER, M.D., University of Minnesota, Minneapolis. Diagnosis of glottic carcinoma. Geriatrics 19:191-195, 1964.

William H. Stewart

Chester A. Stewart

The Stewart Family and the Surgeon Generalship of the United States Public Health Service

J. ARTHUR MYERS, M.D.

To know a person from the day of his birth until he is appointed to the highest public health position in the land is my unique and most gratifying experience. A grand heritage along with methodical, uninterrupted training and years of loyal and devoted service with superb accomplishments led to the September 24, 1965, appointment of William H. Stewart to the Surgeon Generalship of the United States Public Health Service by President Lyndon Johnson. Six days later, the United States Senate confirmed his appointment as the tenth Surgeon General in the one hundred sixty-seven year history of the Service. The appointment of William H. Stewart guarantees the best that is possible through that office for the health of our citizenry and, to considerable extent, for the worldwide citizenry!

The qualities that William H. Stewart brings to the Surgeon Generalship are traceable, in part, to his heritage as the son of a great scholar and physician, Chester A. Stewart. The Stewart family demonstrates in a noble and thrilling manner the old expression "Like father, like son."

The father, Chester A. Stewart,[1] was born on November 6, 1890, in Hannibal, Missouri. When Chester was 14 years old his father died from rheumatic fever. Chester then assumed considerable responsibility for his two brothers, aged 8 and 11, as well as the support of their mother. He accepted any kind of work available outside of school hours. In fact, he frequently began delivering papers shortly after 2 A.M. Following completion of high school, he entered the University of Missouri where he earned his way as a waiter in a boarding club and by doing odd jobs. His clarinet playing proficiency increased his earning capacity while in high school but helped immensely after he entered the University. Having completed the course at the University of Missouri including the first two years of medicine in the spring of 1914, his record merited the awarding of a Shevlin Fellowship at the University of Minnesota under the directorship of the famous anatomist C. M. Jackson. There, in addition to teaching the various anatomical subjects, he engaged in research. He was awarded the degree of Doctor of Philosophy in Anatomy in 1917 and became an instructor in pathology in 1918 under the renowned pathologist, E. T. Bell.

Throughout the years, Chester Stewart took courses in medicine as time permitted and earned the degree of Doctor of Medicine in 1919. He became deeply interested in pediatrics; therefore, he registered in the graduate school and wrote his thesis on "The Vital Capacity of the Lungs in Children in Health and Disease," one of the earliest studies of pulmonary function in this area. In June 1921, he was awarded the degree of Doctor of Philosophy in Pediatrics and promptly was appointed instructor in pediatrics on a part-time basis. He devoted the remainder of his time to private practice. He was one of the most popular teachers in the school of medicine. To his office, he attracted as fine a clientele as any pediatrician ever enjoyed in this city. He ranked high among the pediatricians of America and abroad. In 1941, Dr. Stewart became Chief of the Department of Pediatrics at the Louisiana State University in New Orleans, where he devoted his entire time to teaching and research. He published more than 100 articles in scientific and medical journals. He was an active member of the Editorial Board of The Journal-Lancet from 1929 until his death from coronary occlusion on February 8, 1946.

In September 1914, just before going to the University of Minnesota, Chester Stewart married Miss Dorothy Huffman of Nevada, Missouri. Soon they established a home on an extremely small financial income, but with a dominant spirit to succeed in every aspect of life and to contribute to the good of humanity. Three boys were born into this typical American home which was maintained always as such! On December 28, 1916, their first child, John, was born. Their second, William H., was born May 19, 1921. The day William was born, his father held three degrees and was about to become Doctor of Philosophy in Pediatrics. The third son, James, arrived on June 10, 1926.

As the boys were growing up, Mrs. Stewart was always at home when they returned from school or from any other occasion. They were provided with everything necessary for growth and development, respect of their associates, and respect for themselves. The parents held a taut but not too tight disciplinary rein, knowing the three sons' whereabouts at all times. John became a prominent industrialist, and James a veterinarian who now holds a responsible position with the United States Department of Agriculture in Washington.

William entered Washburn High School where he graduated in 1939. The next two years were spent at the University of Minnesota, and in 1941, when his father became Chief of the Department of Pediatrics at the Louisiana State University, William transferred to that institution and received the degree of Doctor of Medicine in 1945. He then chose the Philadelphia General Hospital for a rotating internship. From 1946 to 1948, he was in the United States Army Corps and for a time served as physician in one of the Veterans Administration's outpatient clinics. From 1948 to 1950, he was a resident in pediatrics at the Charity Hospital, New Orleans. He then launched upon private practice in pediatrics at Alexandria, Louisiana, and rapidly became successful.

William had served less than twenty-one months as a physician during World War II and therefore was subject to the draft when the Korean conflict began. A friend informed him that the Communicable Disease Center was starting an Epidemic Intelligence Service and that they particularly wanted pediatricians because they had more experience with infectious disease. He thought he could make more contributions in the Epidemic Intelligence Service than by returning to the Army as a pediatrician. The United States Public Health Service promptly accepted him and he became a commissioned officer in 1951. His ability was so recognized and appreciated that he was promptly made head of the Epidemiology Unit, Thomasville Field Station, Communicable Disease Center at Thomasville, Georgia. In 1953, he was transferred to National Institutes of Health, National Heart Institute—Grants and Training Branch. Only two years later, he was transferred to the Bureau of States Services, Division of Special Health Services, as Chief, Heart Disease Control Program. This led to the Assistant Directorship of the National Heart Institute, National Institutes of Health. In 1957, he became assistant to the Surgeon General, Public Health Service, and one year later, Chief, Division of Public Health Methods in the office of the Surgeon General, Public Health Service. He became Chief of the Divison of Community Health Services, Bureau of State Services of the Public Health Service in 1961 and two years later assistant to the special assistant to the Secretary (health and medical affairs). In August 1965, he was made Director of the National Heart Institute, National Institutes of Health, approximately a month before his appointment to the Surgeon Generalship.

President Lyndon Johnson truly sought and found a most highly qualified physician for this position.

Dr. Stewart is author of scores of publications and presentations dealing with a wide range of public health issues including spread and control of various diseases, health status of the population, education for the medical and health professions, and medical care administration.

As Surgeon General, he will administer the 100 or more programs of the Public Health Service, with a 1965 budget approximating $2,000,000,000 with a personnel numbering in excess of 38,000 persons.

In June 1946, Miss Glendora White of New Orleans and Dr. Stewart were married. She had also been reared in an ideal American home. In all of his subsequent activities, Mrs. Stewart has played a dominant role. She has not only conducted the ideal American home at 9108 Ewing Drive, Bethesda, Maryland, but has also manifested deep interest in and contribution to the success of Dr. Stewart's many professional projects. Their two daughters, Martha, 16, and Laura, 14, are being reared in the same kind of home and noble heritage as their parents and grandparents.

When informed of Dr. Stewart's appointment, Dr. Thomas J. Heldt, who taught the father, Chester Stewart, anatomy at the University of Missouri and who presently is Director Emeritus, Division of Neuropsychiatry, Henry Ford Hospital, Detroit, wrote: "That is great! Fostered by his rich parental inheritance, he will carve a golden monument of service in his new position and to the high credit of himself and his family background."

"Like father, like son"—I am honored to have known them both!

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CERVICAL AND VAGINAL CANCER can often be detected in only two or three minutes by fluorescence. A hematoporphyrin compound concentrates in the lesions and produces fluorescence under ultraviolet light, demonstrating both the location and extent of the malignant process. The simple procedure is recommended for patients with suspicious or positive postsurgical cytological smears from the vaginal vault. Since the compound may cause a slight, transient photosensitivity, patients should stay out of direct sunlight for three to ten days after the examination. In 51 patients, correlation was good between fluorescent and Schiller-positive areas, and was typical in 29 of 31 malignant lesions proved by biopsy.

RICHARD L. LIPSON, M.D., JOSEPH H. PRATT, M.D., EDWARD J. BALDES, PH.D., and MALCOLM B. DOCKERTY, M.D., Mayo Clinic and Foundation, Rochester, Minn. Hematoporphyrin derivative for the detection of cervical cancer. Obstet. and Gynec. 24:78-84, 1964.

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Book Reviews . . .

The Chemistry and Therapy of Disorders of Voluntary Muscles

by E. G. MURPHY, M.B., *123 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $6.50*

The purpose of this monogram, as stated in the introduction, is to review the main aspects of some of the more important diseases of muscle with emphasis on the biochemical and therapeutic features. The author attempts to accomplish this in a series of short essays, each dealing with one specific muscle disease. The title is misleading for the clinical and pathological features are given attention equal to that assigned the biochemistry and therapeutic.

In a book of this length, the treatment of each disease is necessarily brief. The paragraphs on electromyography and the myopathies related to metabolic disorders suffer most in this respect. The latter are each allotted one short paragraph. By contrast, the introductory chapter, written by Dr. G. R. Williams, gives adequate treatment to the structure and chemistry of the contractile elements. Similar attention to the neuromuscular apparatus and the functional organization of the motor unit would be valuable, but are not included. It soon becomes apparent to the reader that the scope of the theme is too vast to be contained in these few pages. However, the book has merit as a synopsis of the subject.

This book should be attractive to the busy practitioner, to whom it offers a brief review of the major aspects of muscle disorders. For the student, it can serve as an introduction to this group of diseases, to be read before the more complete works are explored. The list of references is inclusive enough to act as an initial guide to many original experimental papers and review sources.

The format of the book is excellent; it is well bound, the printing is easily read, and the illustrations are of high quality.

WILLIAM R. KENNEDY, M.D.
Minneapolis

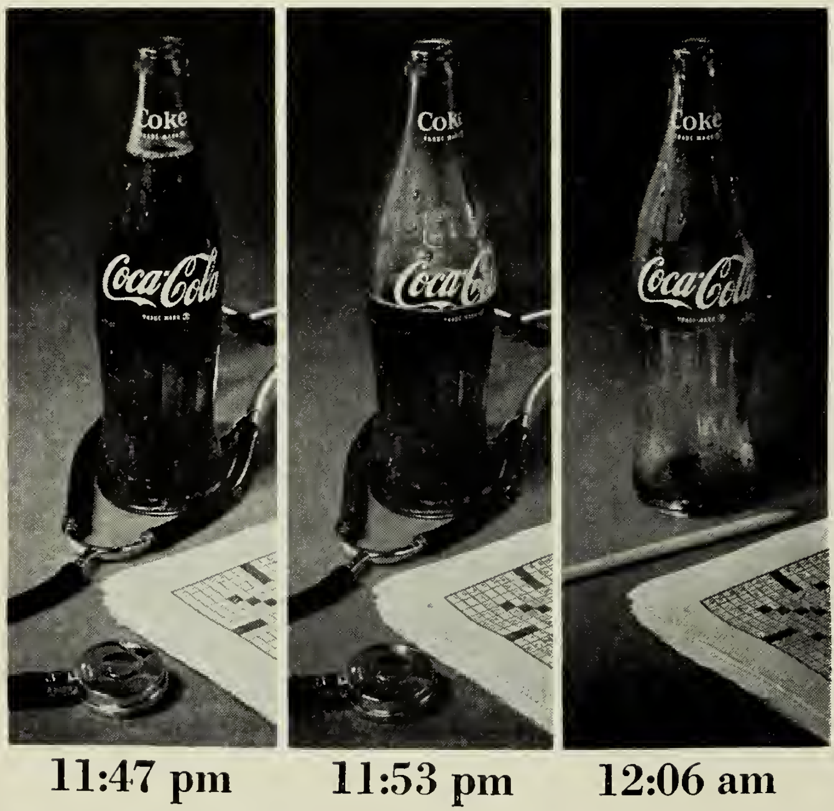
The Practitioner's Illustrated Dermatology

by HOWARD T. BEHRMAN, M.D., *189 pp., ill., Grune & Stratton, Inc., New York, 1965. $9.75*

The stated purpose of this book is to provide physicians and medical students with a simple, small manual of dermatology, and this modest goal has been attained in this short volume. It appears to have been developed around a collection of clinical photographs. Altogether, each of thirty-five common skin diseases is illustrated. On the opposite page is a short paragraph of general comment on the disease illustrated, a few sentences about its clinical features, and a short outline of recommended treatment. At the end of the book is formulary of both internal and external remedies for the various dermatoses.

The illustrations of the dermatoses are all in color and generally are of good quality, giving a demonstration of the diseases in question. Discussion is extremely brief, sometimes necessarily omitting important features of the diseases in question. The reviewer finds the recommended treatment methods generally agreeable to his own ideas, with, inevitably, a few exceptions. Perhaps the most

(Continued on page 19A)



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512214

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BP reductions in the recumbent and sitting positions often are nearly as great as in the standing. In clinical trials, the average *recumbent* BP reduction was 36/18 mm. Hg.

The average *standing* reduction in clinical trials was 45/22 mm. Hg. Thus the difference between the standing and recumbent readings was only 9/4 mm. Hg.

Significantly lowers blood pressure in all body positions; less likelihood of orthostatic hypotension

In clinical trials, the average reduction in standing blood pressure was 45/22 mm. Hg.; in the sitting position it was 48/20 mm. Hg.; and in the recumbent position, 36/18 mm. Hg.

Because Eutron effectively reduces blood pressure in all body positions, there is reduced likelihood of orthostatic symptoms or hypotension.

This was reflected in the relatively mild character of side effects seen in clinical trials (see below).

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Fewer than 1% of patients studied discontinued Eutron therapy because of side effects. This is due in part to the relatively low dosage needed with the combination. Usual recommended dose is one tablet daily—that is, 25 mg. Eutonyl with 5 mg. Enduron. *This is about half the usual therapeutic dose of Eutonyl given alone.* As a consequence side effects may be milder. And, as with Eutonyl given alone, the patient may well note an increased sense of well being. This is in distinct contrast to most other antihypertensive therapy.

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Prescribing information for

EUTRON

INDICATIONS: Eutron (pargyline hydrochloride and methyclothiazide) is indicated in the treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. It is not recommended for use in patients with mild or labile hypertension amenable to therapy with sedatives and/or thiazide diuretics alone.

CONTRAINDICATIONS: Eutron is contraindicated in patients with pheochromocytoma, advanced renal disease, paranoid schizophrenia and hyperthyroidism. Until further experience is gained it cannot be recommended for use in patients with malignant hypertension, children (under 12 years of age), or pregnant patients.

The concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyldopa. A drug-free interval of two weeks should separate therapy and use of these agents.

WARNINGS: Pargyline hydrochloride is a monoamine oxidase inhibitor. Patients should be warned against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When it is necessary to administer alcohol, narcotics (notably meperidine), antihistamines, anesthetics, barbiturates and other hypnotics, sedatives, tranquilizers, or caffeine, these agents can be used cautiously at a dosage of ¼ to ⅕ the usual amount. Avoid parenteral administration where possible. Withdraw pargyline two weeks before elective surgery.

Patients should be warned about the possibility of postural orthostatic hypotension. Those with angina or other evidence of coronary disease should not increase physical activity. Pargyline may lower blood sugar. Potassium depletion is unlikely at the recommended dosage, but if it occurs, adjust dosage or withdraw or provide added natural food sources of potassium; potassium tablets should be avoided wherever possible, as bleeding or obstructive ulceration of the small bowel has been associated with their use; potassium levels should be especially watched if the patient is on digitalis or steroids, or if hepatic coma is impending.

PRECAUTIONS: When determining the antihypertensive effect of Eutron, blood pressure should be measured while the patient is *standing*. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Pargyline has not been shown to cause damage to body organs or systems. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. The drug should be used with caution in patients with liver dysfunction. With prolonged therapy, examine patients for change in color perception, visual fields, and fundi.

Elevated blood urea nitrogen, serum uric acid or blood sugar are possibilities attributable to the methyclothiazide in Eutron. Methyclothiazide may also reduce arterial response to pressor amines. Blood dyscrasias, including thrombocytopemia with purpura, agranulocytosis and aplastic anemia, have been seen with thiazide drugs.

SIDE EFFECTS: The use of pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extra-pyramidal symptoms have been reported. Drug fever is extremely rare. Congestive heart failure has been reported in a few patients with reduced cardiac reserve. Nocturia has been observed with the combination. If side effects persist, despite symptomatic therapy or reduction of the dose, discontinue the drug.

ABBOTT

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(Continued from page 14A)

important reservation he would have about the telegraphic style used in suggesting therapy in this book, is that it is not always possible to emphasize the hazards attendant on use of some of the recommended treatment methods, some of which might not be sufficiently well-known to the relatively unsophisticated medical public for whom this book is evidently designed. Thus, while the danger to the eyes attendant on use of chloroquine is mentioned very briefly, the use of this hazardous agent is recommended for a number of conditions, some quite minor in nature. The danger of extensive and disfiguring depigmentation after use of benzoquinone is not mentioned at all, nor is much emphasis given to some of the undesirable consequences of intralesional injection of corticosteroids in the undiluted form. Generally, proprietary names of drugs are used in preference to generic names, and often the choice of recommended drug appears to have been quite arbitrary. In general, however, the methods of treatment described are up-to-date and meet the standards of good current dermatologic therapy.

This book certainly is not intended for dermatologists, or for that matter, for any physician who has more than the most superficial interest in skin diseases. Its "cook book" approach will probably make it of value to general physicians who need a handy atlas to refer to for quick help in diagnosing an eruption or deciding on treatment for it. As noted, only the most common dermatoses are considered and textual material is extremely brief. The reviewer is reminded of those manuals which were published to aid armed forces medical officers during World War II. This book, though even briefer than those manuals, might, with its excellent illustrations of common skin disorders and its concise recommendations for therapy, be very useful. For physicians wanting such a brief handbook, this book can be recommended.

ROBERT W. GOLTZ, M.D.
University of Colorado, Denver

BOOKS RECEIVED

Physiology of Exercise by ERNST JOKL, 145 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $6.50

First Aid: Diagnosis and Management by WARREN H. COLE, M.D., and CHARLES B. PUESTOW, M.C., 6th ed., 445 pp., ill., Appleton-Century-Crofts, New York City, 1965. $6.95

Clinical Orthopaedics and Related Research No. 30—Fractures of the Tarsal Bones, editor-in-chief, ANTHONY F. DE PALMA, and guest editor, CHARLES S. NEER II, M.D., 251 pp., ill., J. B. Lippincott Co., Philadelphia, 1963. $8

Clinical Orthopaedics and Related Research No. 31—Osteoarthrosis of the Hip Joint and Its Management, editor-in-chief, ANTHONY F. DE PALMA, 269 pp., ill., J. B. Lippincott Co., Philadelphia, 1963. $8

(Continued on page 20A)

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BOOK REVIEWS

(Continued from page 19A)

Nutrition, Exercise, and Body Composition, by ERNST JOKL, 115 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $5.75

The Lymphatics of the Female Genital Organs by GUNTHER FEIFFENSTUHL, 165 pp., ill., J. B. Lippincott Co., Philadelphia, 1964. $10

Animals Parasitic in Man by GEOFREY LA PAGE, rev. ed., 320 pp., ill., Dover Publications, Inc., New York City, 1963. $1.85

Heart and Sport by ERNST JOKL, 117 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $6

Bronchitis, edited by N. G. M. ORIE, M.D., and H. J. SLUITER, M.D., 358 pp., ill., Charles C. Thomas, Springfield, Ill., 1965. $17.50

Cardiomyopathies, edited by G. E. W. WOLSTENHOLME, F.R.C.P., and MAEVE O'CONNOR, B.A., 428 pp., ill., Little, Brown and Co., Boston, 1964. $12.50

Chinese Lessons to Western Medicine by I. SNAPPER, M.D., Second Edition, 416 pp., ill., Grune & Stratton, Inc., New York, 1965. $12.00

Early History of the Ochsner Medical Center: The First Twenty-Two Years by GUY A. CALDWELL, M.D., 115 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $4.75

Health Organizations of the United States, Canada and Internationally by CLARA SEDACCA WASSERMAN with PAUL WASSERMAN, 261 pp., ill., Graduate School of Business and Public Adm., Cornell University, Ithaca, New York, 1965. $13.50

Mental Testing in Clinical Practice by MOYRA WILLIAMS, M.A., 177 pp., Pergamon Press, New York City, 1965. $3.50

A Primer of Cardiac Catheterization by ROSS C. KORY, M.D., THEOFILOS, J. TSAGARIS, M.D., and RODRIGO A. BUSTAMANTE, M.D., 114 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $7.50

A Primer of Water, Electrolyte and Acid Base Syndromes by EMANUEL GOLDBERGER, M.D., 3rd edition, 410 pp., ill., Lea and Febiger, Philadelphia, 1965. $6.50

Synopsis of Contemporary Psychiatry by GEORGE A. ULETT, M.D., and D. WELLS GOODRICH, M.D., 299 pp., C. V. Mosby Co., St. Louis, 1965. $6.75

Textbook of Parasitology by DAVID L. BELDING, M.D., 3rd ed., 1374 pp., ill., Appleton-Century Crofts, New York City, 1965. $17.95

News Briefs . . .

North Dakota

PROJECT VIET NAM signed Dr. Charles A. Rodman II of the U.S. Air Force Hospital at Minot for a two-month tour with South Viet Nam medical teams. He was scheduled to return in February.

* * * *

DR. JAMES R. AMOS of Bismarck, the state's chief health officer, has been reappointed to a second four-year term by Gov. William L. Guy.

* * * *

DR. PETER MORRISON of Eastend, Sask., plans to open a clinic at Towner early this year.

Minnesota

DR. VICTOR M. COLAGO, a graduate of the University of Santo Tomas, Manila, has become the first physician in three years to practice medicine in Browns Valley. He was in Winnipeg when the state department reversed an earlier immigration ruling, enabling him to accept an offer from Browns Valley civic leaders to practice there.

* * * *

DR. ROBERT V. HODAPP of Willmar has been elected a Fellow of the American Academy of Pediatrics. He is a graduate of the University of Minnesota Medical School.

* * * *

DR. BRUCE W. WELLS of Worthington has begun a tour of duty as a Navy flight surgeon. He had been associated with the Worthington Clinic.

* * * *

DR. JOHN W. FODERICK, a graduate of the University of Western Ontario, London, Ont., is associated with Dr. Herman J. Just in general practice at Hastings.

* * * *

DR. WILLIAM R. FIFER of the St. Louis Park Medical Center has been elected president of the Minnesota Thoracic Society. Thus, he also becomes a member of the executive board of the Minnesota Tuberculosis and Health Association.

* * * *

DR. BRIAN J. MC GROARTY of St. Paul has succeeded Dr. Eugene E. Scott as president of the Ramsey County Medical Society. The president-elect is Dr. John R. Earl of South St. Paul.

* * * *

DR. WILLIAM J. KOZEL of Morris has been elected president of the West Central Minnesota Medical Society, succeeding Dr. Robert M. Watson.

* * * *

DR. GEORGE A. HALLENBECK has been named president-elect of the voting staff at the Mayo Clinic. Dr. Hallenbeck, head of the surgical research section, will succeed Dr. Collin S. MacCarty in the presidency next year. Dr. MacCarty is chief of neurologic surgery.

* * * *

DR. JACK A. NAROS has started a full-time practice at the Crosby Clinic.

(Continued on page 22A)

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FREE PARKING

(Continued from page 21A)

DR. DAVID W. FEIGAL of Wayzata is starting an eighteen-month term as president of the Hennepin County Academy of General Practitioners.

* * * *

DR. PAUL D. RUD has been elected chief-of-staff at Luverne Community Hospital. He is a graduate of the University of Wisconsin Medical School.

* * * *

A 12-member National Advisory Council appointed by President Johnson includes Dr. Clark H. Millikan of the Mayo Clinic. The council will study regional medical programs.

* * * *

DR. DENNIS J. KANE, suspended earlier from his post as director of medical education at St. Paul-Ramsey Hospital, has been reinstated as a member of the executive committee. An announcement from hospital officials said differences between members of the staff had been resolved, and that the position of director of medical education, which carried certain responsibilities without real authority, is being redefined.

* * * *

TWO PHYSICIANS from Waseca are moving to new localities. Dr. Wayne L. Campbell announced plans for practicing in Novato, Calif., and Dr. L. Eugene Stover said he would move to Marshall, Minn.

* * * *

THE PUBLIC HEALTH SERVICE has awarded a $24,447 grant to Dr. David M. Witten of the Mayo Foundation for the training of radiologists, residents, and technicians in mammography.

* * * *

GRANTS TOTALING $500,000 will enable the St. Paul Medical Center to operate into 1970, according to Dr. Winston R. Miller, medical director. The grants are from the Amherst H. Wilder and Louis and Maud Hill Foundations. The center was established by 5 voluntary hospitals for research, training, and a part-pay medical care program for indigent patients.

* * * *

DR. NORMAN W. HOOVER, Mayo Clinic orthopedic surgeon, volunteered to spend two months in South Viet Nam treating war-injured civilians and others. His stay was scheduled through December and January.

South Dakota

DR. HAROLD L. FROST of Rapid City has been elected president of the Black Hills District Medical Society. Dr. Theodore R. Jacobson of Hot Springs was elected vice-president, and Dr. John M. Hewitt of Rapid City was reelected secretary-treasurer.

* * * *

DR. ARTHUR A. LAMPERT of Rapid City has been appointed to a national committee of consultants assisting the Social Security Administration in the formulation of Medicare procedures.

* * * *

DR. ISAIAH R. SALLADAY, 71-year-old staff physician at the Veterans Administration Hospital, Fort Meade, signed for a two- to three-month tour with Project Viet Nam in South Viet Nam.

(Continued on page 24A)

DEPROL®

meprobamate 400 mg. +
benactyzine hydrochloride 1 mg.

Indications: 'Deprol' is useful in the management of depression, both acute (reactive) and chronic. It is particularly useful in the less severe depressions and where the depression is accompanied by anxiety, insomnia, agitation, or rumination. It is also useful for management of depression and associated anxiety accompanying or related to organic illnesses.

Contraindications: Benactyzine hydrochloride is contraindicated in glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

Precautions: *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

Benactyzine hydrochloride—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

Meprobamate—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Dosage: Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

Supplied: Light-pink, scored tablets, each containing meprobamate 400 mg. and benactyzine hydrochloride 1 mg.
Before prescribing, consult package circular.

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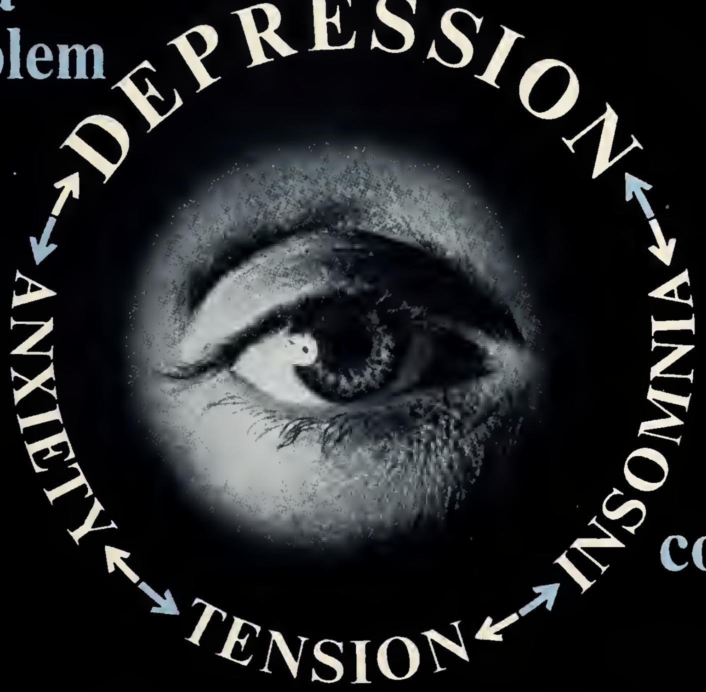

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WANTED—Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty-seven bed hospital with X-ray and laboratory technicians and nurse anesthetist. Good hunting and fishing. Adequate salary and time off. Contact A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

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GENERALIST NEEDED—Death of associate in three man group in General Practice in White Bear Lake, Minnesota requires immediate replacement. Salary with advancement to partnership negotiable. Excellent opportunity for young man in an established practice of young men (under 38 years old). New building in suburban area of St. Paul. Locum tenens also considered. Write A. J. Rushay, M.D., or T. G. Briggs, M.D., c/o Journal Lancet, Box 38.

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(Continued from page 22A)

Deaths . . .

DR. OLAF J. HAGEN, 93, a resident of Moorhead, Minn., since 1873, died Dec. 3 in a nursing home at Fargo, N.D. Dr. Hagen, at 19, was a history instructor at Concordia College, later attended St. Cloud State College, the University of North Dakota, and was graduated from the University of Minnesota Medical School in 1906. He did postgraduate work at Harvard College and the University of Berlin, and was founder of the Fargo Clinic. A member of the International College of Surgeons, he was on the surgical staff at St. Luke's Hospital for thirty years. Dr. Hagen established the first consolidated school west of Illinois and at one time was superintendent of schools in Richland County, N.D.

* * * *

DR. ALMER M. AANES, 79, died Nov. 28 at St. John's Hospital in Red Wing, Minn. Dr. Aanes was graduated from Hahnemann Medical College and Hospital of Philadelphia in 1909 and had practiced in Red Wing from 1912 until 1955. He was chief-of-staff at St. John's Hospital for 1 term and served as Goodhue County health officer for many years.

* * * *

DR. JOHN E. TWOMEY, 45, chief-of-staff at St. Mary's Hospital, Minneapolis, died of cancer at his home Nov. 30. Dr. Twomey received his degree from the University of Minnesota Medical School in 1946. He was a member of the American Board of Surgery and had served as chief-of-staff at St. Mary's since 1962. Dr. Twomey also was a member of the Glen Lake Sanatorium Commission, the General Hospital and Health Advisory Board, and the governing board of the Minneapolis War Memorial Blood Bank.

* * * *

DR. CARL G. ARVIDSON, 74, of Minneapolis, died Dec. 12. He was a graduate of the University of Minnesota Medical School and a member of the staff at Swedish Hospital, Minneapolis. Dr. Arvidson was a supervisor in venereal disease diagnosis at state institutions.

* * * *

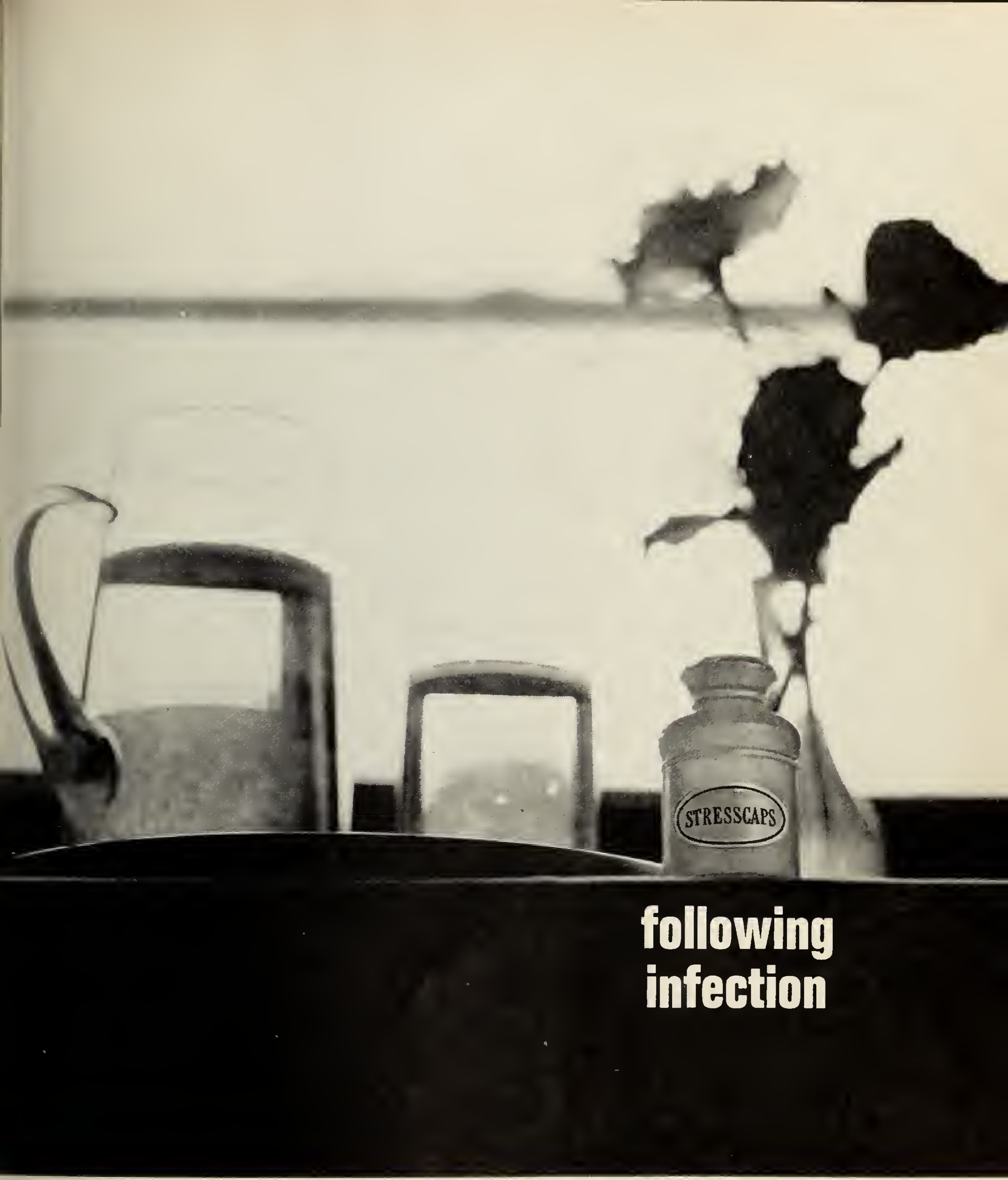
DR. CARL B. DRAKE, 79, former president of the Minnesota Medical Association, died Dec. 9 at his home in St. Paul. Dr. Drake had served as an officer in the state association from 1921 until 1959 when he resigned because of ill health. He was a member of the Ancker Hospital staff for forty years and was school physician at St. Paul Academy for thirty-four years. He was graduated from the University of Minnesota Medical School in 1912.

* * * *

DR. FLOYD A. THOMPSON, 62, a general practitioner in St. Paul for thirty-four years, died Nov. 24. Dr. Thompson was a graduate of the University of Minnesota Medical School and a former chief-of-staff at St. Luke's Hospital.

* * * *

DR. WILLIAM J. MARTIN III, 65, former Louisville, Ky., surgeon, died Dec. 10 at Rochester, Minn. A former Fellow in the Mayo Graduate School of Medicine, Dr. Martin had been in retirement since 1963. Death was due to cancer.



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Niacinamide	100 mg.
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Vitamin B_6 (Pyridoxine HCl)	2 mg.
Vitamin B_{12} Crystalline	4 mcgm.
Calcium Pantothenate	20 mg.

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...brings more blood and oxygen to the myocardium *safely*

...stimulates development of collateral circulation[4]

Side effects: Negligible—but, occasionally, transient headache may occur.

Precautions: Exercise caution in glaucoma, and with dosage forms containing phenobarbital, which may be habit forming. Full information available on request.

References: 1. Johnson, P. C., and Sevelius, G.: J.A.M.A. *173*:1231, 1960. 2. Data on file in the Medical Department, Warner-Chilcott Laboratories. Available on request. 3. Sadove, M. S.; Rosenberg, R.; Heller, F., and Shulman, M.: Am. Prof. Pharm. *31*:23, 1965. 4. Lumb, G. D., and Hardy, L. B.: Circulation (Pt. II, Cardiovascular Surgery) *27*:717, 1963.

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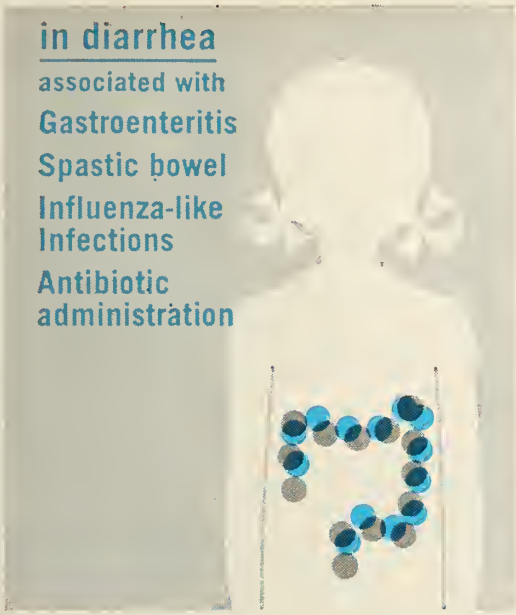

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1. Janssen, P. A. J., and Jageneau, A. H.: A New Series of Potent Analgesics: Dextro 2:2-Diphenyl-3-Methyl-4-Morpholinobutyrylpyrrolidine and Related Amides. Part 1: Chemical Structure and Pharmacological Activity, J. Pharm. Pharmacol. 9:381-400 (June) 1957.

2. Demeulenaere, L.: Action du R 1132 sur le transit gastro-intestinal, Acta Gastroent. Belg. *21*:674-680 (Sept.-Oct.) 1958.

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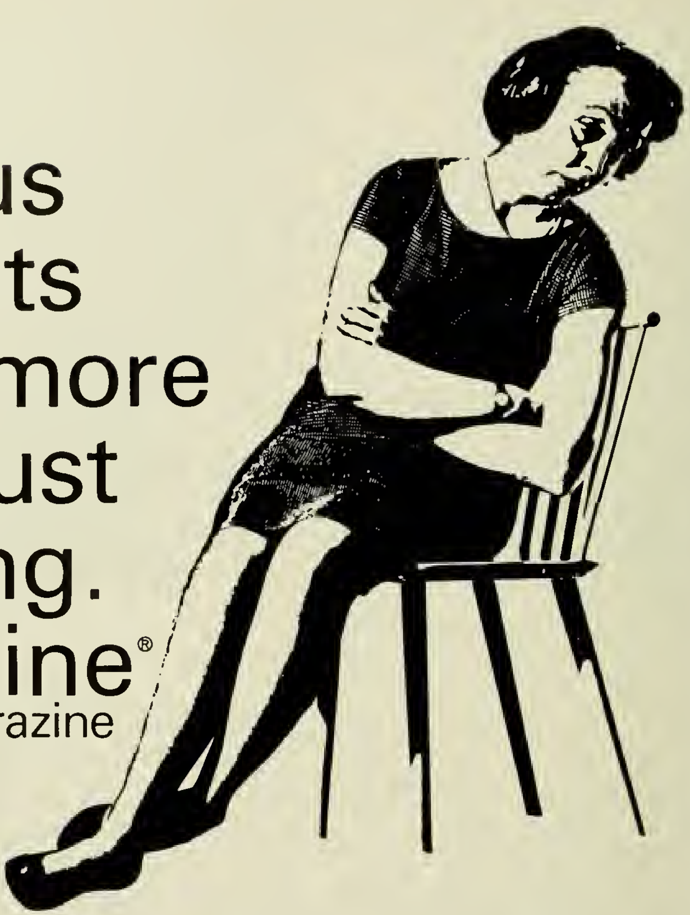

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The Journal-Lancet Volume 86, No. 3, MARCH 1966

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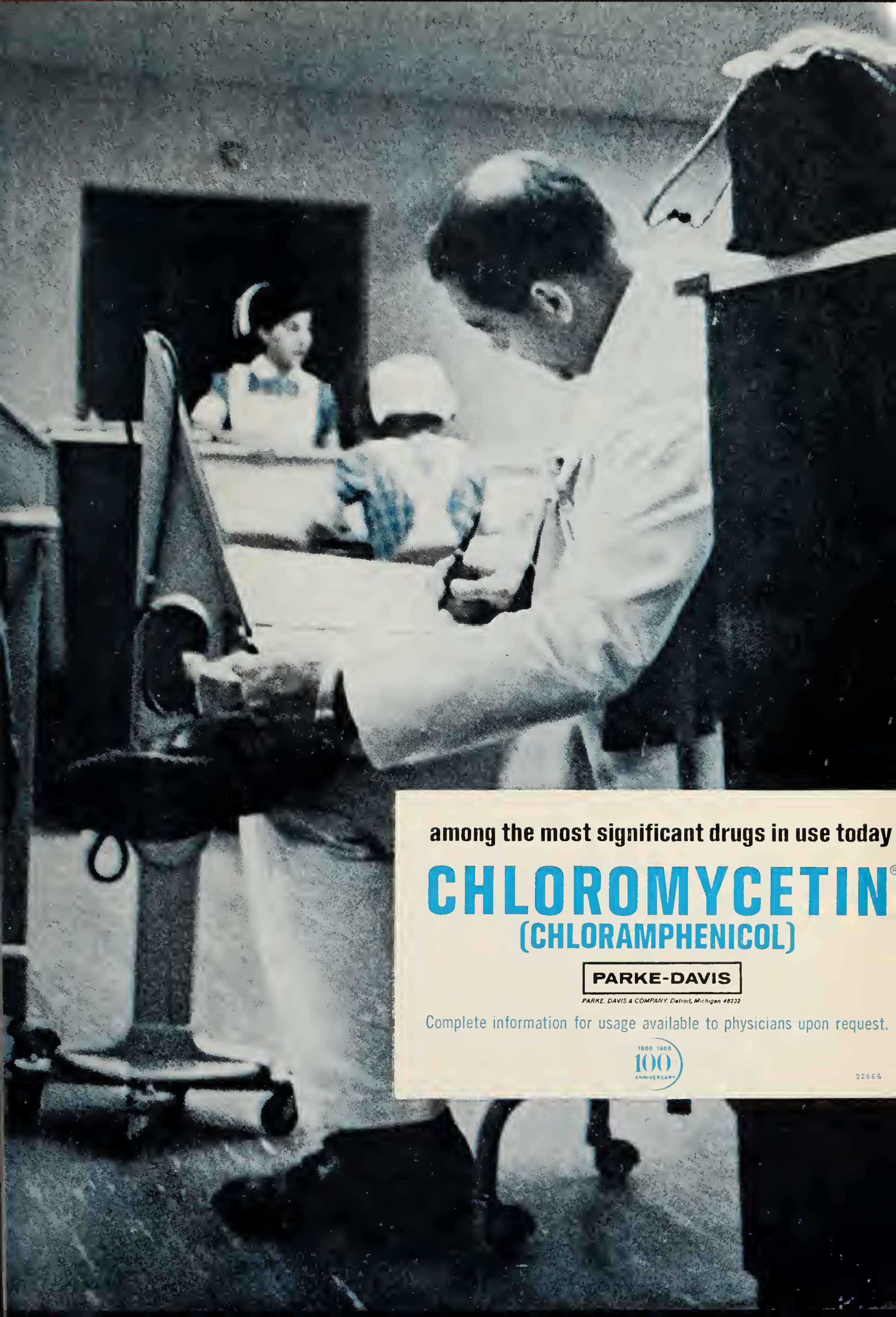

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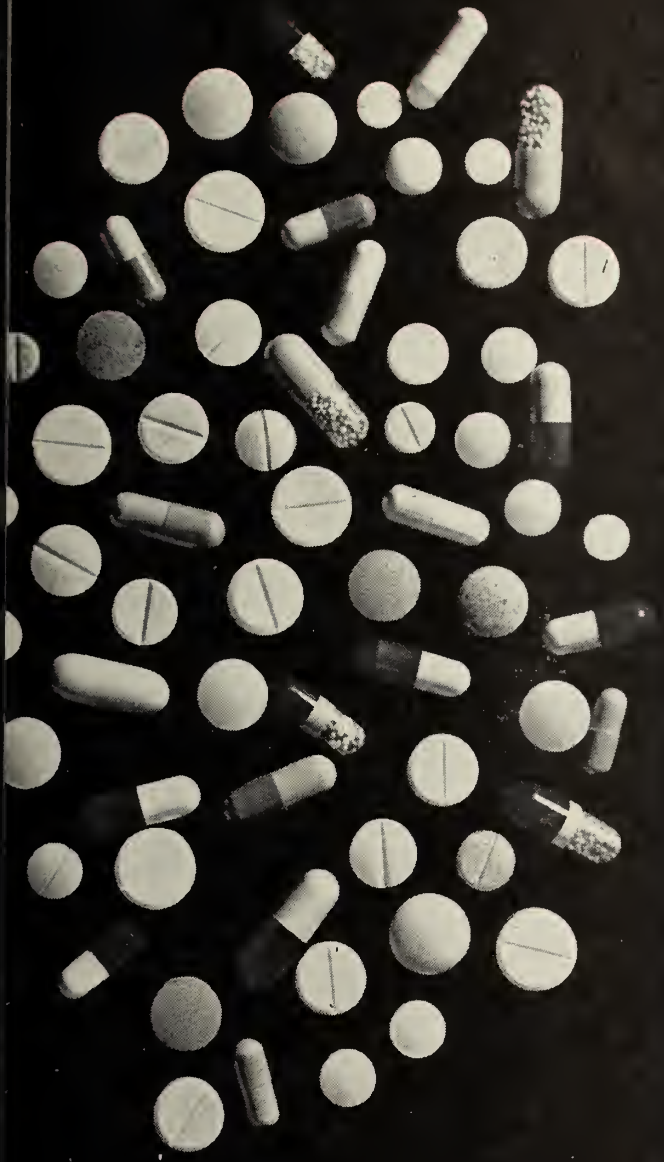

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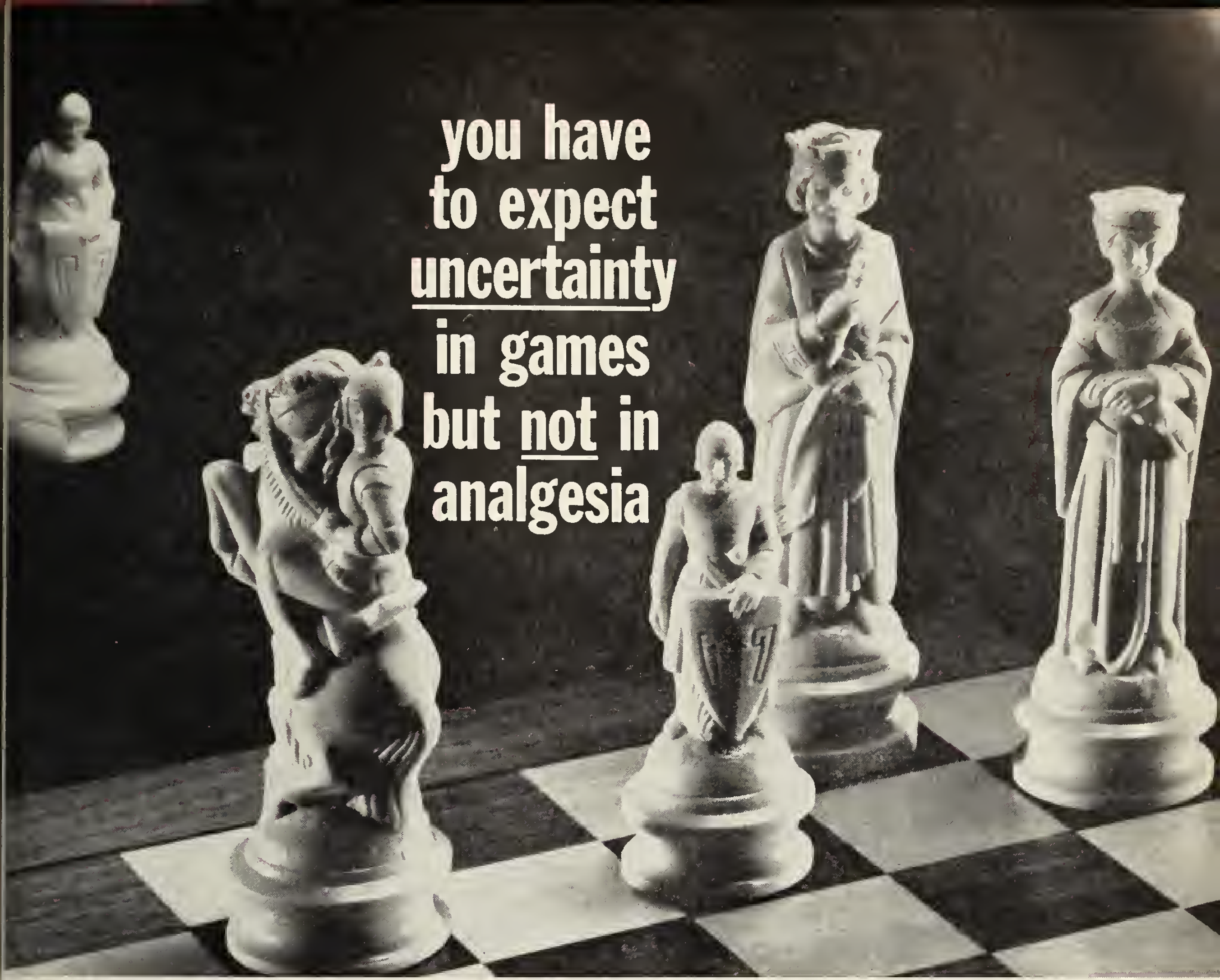

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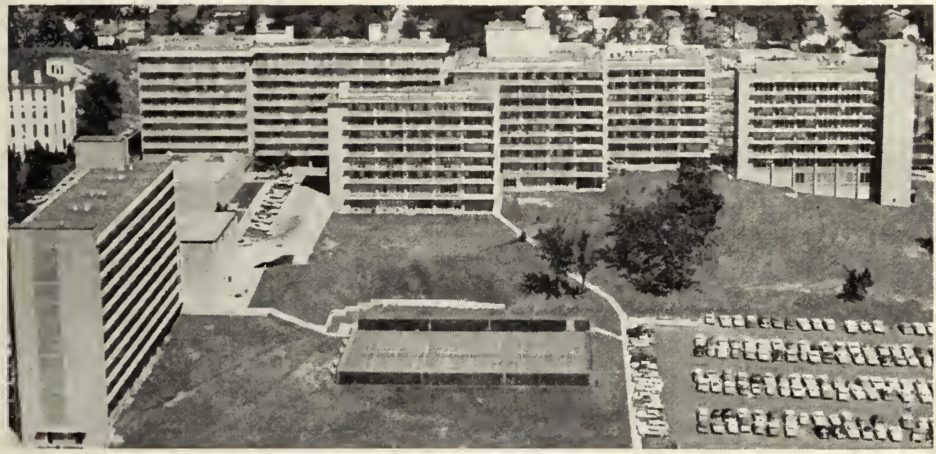

Prefatory Remarks

The department of pediatrics of the University of Arkansas Medical Center welcomes the opportunity to sponsor this "Arkansas" issue of THE JOURNAL-LANCET and thus to join the community of medical centers featured in similar special issues. Although the University of Arkansas was incorporated as a land grant college in 1871, the medical center as currently constituted is of recent origin, and the following brief descriptive account may therefore be of interest.

The present school of medicine of the University of Arkansas, which serves a state population of about 1.8 million, dates back to 1911 and resulted from the merger of 2 self-supporting medical schools which were opened in 1879 and 1906, respectively. It occupied the famous antebellum state capitol building until 1935, when it moved to newly constructed quarters adjacent to the city hospital, which soon became the official teaching hospital of the medical school. Following the close of World War II, the need for expansion of programs and facilities became increasingly apparent and, under admirable leadership of a nucleus of farsighted professional and lay citizens, the state legislature in 1949 authorized construction of a new medical center and started a building fund. Two years later the

1951 legislature voted a two-cents-a-package increase in the state cigarette tax to add support to the overall project, and funds thus derived served as the financing base for the medical center's building years.

The present medical center, pictured above and completed at an overall cost of approximately twenty million dollars, was officially dedicated in April, 1957. The basic distinctive architectural design was the work of the noted architect, Edward Durell Stone, a native Arkansan. Although over fifteen years have elapsed since original plans were made, the center still retains a most attractive and contemporary appearance. Represented within the center, in addition to a 450-bed hospital, are the schools of medicine, nursing, pharmacy, medical technology, and X-ray technology. Plans for considerable expansion in scope and extent of activities in medical and paramedical areas are actively under way.

Until 1948 the clinical faculty of the school of medicine was entirely voluntary. In that year pediatrics was established as the first full-time teaching department, largely through the assistance of the Children's Bureau and the Arkansas State Department of Health, with the appointment of Dr. William A. Reilly as chairman. Since that time all clinical departments have been established on a completely full-time basis. Dr. Reilly was succeeded in 1953 by Dr. Katherine Dodd, who was succeeded by the present incumbent in January 1958.

In recent years the number of entering medical students has been raised from 90 to 105. The total student body is in excess of 600, whereas the total full-time faculty is approximately 160. Graduate programs at the masters and doctorate levels are also active in a variety of fields. Research facilities and activities have broadened greatly and monies derived from various granting agencies for such purposes total approximately three million dollars annually.

This "capsule" history of the University of Arkansas Medical Center is offered to familiarize the readers with the institution, as well as with some of the activities within the department of pediatrics, as reflected in the contents of this issue.

THEODORE C. PANOS, M.D.
Professor and chairman, department of pediatrics
University of Arkansas Medical Center

Nutritional Counseling of the Pediatric Patient

MARGARET T. YOUNATHAN, Ph.D.

Little Rock, Arkansas

As PHYSICIANS concerned with the optimal health of children, pediatricians must be constantly alert to nutritional needs and practices. The role of nutrition in pediatrics has been characterized by Holt:[1] "Nutrition in its broadest sense is one of the most important branches of pediatrics. Not only has the growing child exceptional requirements for nutrients; he is also peculiarly vulnerable to disturbances which interfere with his obtaining them." The family physician, because of his broad knowledge of all aspects relating to child health, is regarded as an authority and his advice on what to feed children is readily sought and accepted.[2] Parents are often confused and perplexed by the mass of information presented to them by communications media such as television, radio, newspapers, and magazines, much of which is characterized by commercialism and "the hard sell." Even well-meaning publications in lay periodicals on "how to feed your child" leave parents befuddled and tend to create a compulsiveness or anxiety to meet maximum critera, thus obscuring basic principles of biologic variability and individualization of approach. Nutritional counseling of the pediatric patient, therefore, becomes primarily a matter of guiding parents in discovering that which is desirable for their children and of reconciling the sometimes conflicting advice they receive. The parents, in turn, are able to work more effectively with their children.

Since the patients in question are children, one always is guided by the common denominator of growth and development. All children, regardless of whether they are sick or well, still strive as best they can to accomplish the growth and development tasks of childhood.[3] Providing a diet which is nutritionally adequate helps the child achieve proper growth and development.

Thinking in terms of ages and stages, as suggested by Stitt,[3] helps one keep growth and development needs in mind. Infancy is characterized by the demands of rapid growth and maturation of the mechanisms of food ingestion. In the preschool years, growth is slower but physical activity is almost constant, increasing food requirements and, to many parents' dismay, diverting time and interest for eating. Many dietary problems which are carried over into adult life have their onset in infancy and early childhood. The schoolchild is very active also; he tends toward increasing stockiness with slower linear growth. Adolescence represents the final growth phase. Excess consumption of high caloric beverages, omitting one or even two meals a day, particularly breakfast, obesity, and, perhaps, skin conditions are some dietary problems common to this age group.

Aside from the special diets of the very young or the therapeutic regimen of the sick child, most children do best when their care and feeding are tied in with the total family plan for care and feeding, with emphasis on naturalness and enjoyment.[4] This is the most logical approach from the mother's point of view and may have the added advantage of widening the dietary scope of the entire family.

Any counseling which is done must be offered within the framework of the family's social and cultural background. A study of attitudes, beliefs, and practices surrounding food may constitute an important technique in discovering deeper medical or social problems.[5] Cultural heritage, family background, patterns of food preparation and service, religious customs, and previous emotional experiences with food, as well as exposure to advertisements via mass media, all contribute to the individual's attitude toward and acceptance of food.[6] From the day of birth, food is associated with specific feelings and emotions completely apart from its nutritional significance. Thus, diets as milk, custards, and creamed or strained foods, often used in infant feeding, may convey in some individuals such feelings as security, love, or dependency while being associated in others with rejection, deprivation, or pain.

Food habits develop slowly over the years and

MARGARET T. YOUNATHAN *is assistant professor of pediatrics, Department of Pediatrics, University of Arkansas Medical Center, Little Rock.*

become a deeply ingrained part of one's total self. Attempts to change long-established patterns in the adult may meet with resistance, but in the pediatric patient, one is dealing with a more flexible individual with few preconceived ideas and prejudices. Changes can be made in his nutritional pattern insofar as the adult parent is cooperative in carrying out suggestions relating to dietary regimen. It may be helpful at times to remind parents that the adult controls the environment and to emphasize that his main responsibility is to provide enjoyable and nutritious foods but to limit the amount of highly refined carbohydrate as candies, soda beverages, pies, cakes, and so forth, made available.

In deciding on an approach to nutritional counseling for the child, the physician should utilize ideas and resources of the mother. If it is possible to encourage and support an approach or idea which originated with the mother, or some modification of it, this approach probably has the best chance of succeeding in that particular home. Moreover, by adopting it, the physician engenders confidence in the mother when she is supported by him in her plan.[7]

The physician may wish to take a dietary history of the kinds and amounts of foods that have been eaten by the patient during the previous twenty-four-hour period. This serves to indicate general adequacy of the food intake and a starting point for nutritional counseling. The recorder should be careful to list all beverages and accessories as cream, butter, sugar, jelly, sauces, and so forth. If there appear to be obvious omissions, questions such as "What did you drink with your lunch?" or "What did you have on your bread?" may serve as reminders. Questions should be easily understood, acceptable, and "open-ended," in the sense that they cannot be answered with a direct yes or no. The physician should try to eliminate his own standards and food pattern from his manner of questioning. Otherwise, mothers may answer in accord with his expectations rather than responding freely.[7] If the food intake is not typical of the child's usual eating practices, differences should be noted. Weekends are usually atypical. One may evaluate the adequacy of the food intake by comparing it with Table I. This will suggest areas for emphasis in nutritional counseling.

As one may note from the table, emphasis should be placed on the four fundamental food groups, namely: milk group, meat group, vegetable-fruit group, and bread-cereal group. Additional servings of these foods or others as fats, oils, or sweets may be added for caloric adequacy and satiety. The liberal use of fundamental foods will ensure nutritional adequacy and continued stress should be placed on their consumption. The supplementary foods provide chiefly calories and flavor. Overconsumption of these lead easily to obesity and, in addition, may induce an environment of fermentable carbohydrate, an important caries-contributing factor.[8]

It is easier by far to establish good food habits during infancy and the preschool years than to try to change the long-established, deeply ingrained food patterns of an older child or an adult. The fertile field for nutrition education lies within the age groups of infancy, preschoolers, and the early elementary school years. Establishing good food habits requires teamwork from the physician, nutritionist, teachers, and parents.

Physicians can be helpful to parents by alerting them to problems and situations which are encountered frequently in child feeding. The following suggestions derived from multiple sources[9,10] have been found useful.

[1] Try to see food as children see it. Children are not small adults and have quite different tastes and preferences than adults. [2] Appetite shows considerable variations. Children may be expected to have an occasional loss of or decrease in appetite. This regularly occurs during the second year of life and almost without exception at the onset of any illness. Variations in the quantity of food eaten at different times should occasion no concern. Feeding difficulties arise when parents attempt to standardize a child's food intake. [3] Do not force anything on the child. It is easier to change the food than to change the child. Let the child decide how much to eat. [4] Habits vary from day to day and from meal to meal. Preferences are unpredictable and seem to go in "waves." Allowing a choice of two foods of comparable nutritive value, as between two fruits or two vegetables, sometimes works well for these children. [5] Children prefer mildly flavored and lightly seasoned foods. Mildness is especially important when considering vegetables, fruits, and organ meats for children. [6] Small servings (with seconds available) are preferable to the large servings customarily dispensed by adults and give the child a feeling of accomplishment when he is able to eat everything which he is served. [7] Children are not venturesome in regard to food. They are not gourmets. Keep foods simple. In general, they prefer foods at lukewarm temperature and those of soft, jellylike texture. Finger foods are popular. [8] Recognize that each child is an individual with personal likes and dislikes. [9] Refusing to eat is a weapon of strength for a

TABLE I

A RECOMMENDED DAILY FOOD PATTERN*

Food groups	*Amounts*	*Sources and equivalents*
I. Fundamental foods		
Milk group	Children under 9 years—2 to 3 cups Children 9 to 12 years—3 or more cups Teenagers—4 or more cups Adults—2 or more cups Pregnant women—3 or more cups Nursing mothers—4 or more cups	Calcium value of 1 cup milk: 4 oz. (½ cup) of undiluted evaporated milk, 4 tablespoons of nonfat dry milk, 1⅓ oz. of cheddar cheese, 1½ cups of cottage cheese, 2 cups of ice cream, or 1 glass milk used on cereal or in milk desserts
Meat group	2 or more 3-oz. servings	Best sources: lean beef, veal, lamb, pork, poultry, fish, shellfish, eggs, or variety meats as liver, heart, or kidney Protein value of 3 oz. of cooked meat: 3 eggs, 3 frankfurters, 3 oz. of cheddar cheese, ¾ cup of cottage cheese, 5 tablespoons of peanut butter, or 1½ cups of cooked beans, peas, or lentils Other equivalents: One-pound hamburger yields 4 cooked, 3-oz. servings; 2 pieces of chicken (drumstick and half breast) yield 3 oz. of cooked meat; and mixed meat or meat substitute dishes such as macaroni and cheese, spaghetti with meat sauce, or noodles with tuna usually provide only 2 oz. of meat equivalent per serving. One bread and 1 fat equivalent should be counted for mixed dishes.
Vegetable-fruit group 4 or more servings (½ cup cooked vegetable or 1 raw unit of fruit)	A. One dark green or deep yellow vegetable at least every other day	A. One-half cup of the following cooked foods provides 5,000 I.U. of vitamin A or more: broccoli, spinach, chard, collards, cress, kale, turnip greens, beet greens, mustard greens, carrots, winter squash, sweet potato, or cantaloupe.
	B. One citrus fruit or other vitamin C rich source daily	B. Foods providing approximately 70 mg. of vitamin C: ½ grapefruit; 1 medium orange; ½ cantaloupe; ¾ cup of strawberries; ½ cup of orange, grapefruit, or blended citrus juices; 1 cup of tangerine juice or 2 tangerines; 1 cup of tomato juice; 2 medium raw tomatoes; ½ cup of cooked broccoli, brussels sprouts, or kale; 1 cup of cooked collards, mustard greens, or turnip greens; or ¾ cup of cooked or 1 cup of raw cabbage
	C. Other fruits and vegetables	C. One unit or ½ cup: apples, bananas, apricots, peaches, or potatoes
Bread-cereal group	4 or more servings of enriched or whole grain	Foods equivalent to one serving: 1 slice bread, ½ to ¾ cup of cooked cereal (rice, grits, oats, wheat, macaroni, noodles, or spaghetti); 1 oz. (about 1 cup) of ready-to-eat cereal; 1 roll, muffin, or biscuit; 5 saltine crackers; or 2 graham crackers
II. Additional foods	Servings as needed to meet individual caloric needs and to add variety, flavor, and satiety	Fats and oils, sweets, unenriched cereals, and flavorings

*Derived from multiple sources[9,11,12]

child. The attention commanded from concerned adults contributes to the power of the tool. Refusals are sometimes initiated by the child when he is forced to eat while ill or overtired. [10] Eating habits and patterns are handed down from parents to children. Parents should understand that they must set a good example for the child.

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LONG-TERM PROGNOSIS FOR SCHIZOPHRENIA is poor, even when the initial response to treatment is good. Improvement is most likely to be maintained if the patient is treated actively, preferably with chlorpromazine (Thorazine®). Rapid and recent onset of illness, good former occupational adjustment, and ability to act out in the environment are good signs for short-term prognosis, but there are few signs of value in predicting long-term prognosis.

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Temperature Adaptation of the Newborn to the Extrauterine Environment

D. A. FISHER, M.D., and E. J. MAKOSKI, B.S.

Little Rock, Arkansas

THE RESOURCES of the newborn infant for defense against the acute cold stress precipitated by his abrupt introduction to the extrauterine environment are impressive. His handicaps in this regard, especially if he is premature, are also formidable. The balance achieved among these factors creates a unique pattern of endocrine and metabolic events in the neonate which only recently have been recognized as cold defense mechanisms. It is the purpose of the present paper to review the rapidly accumulating information regarding these neonatal cold responses and to reconstruct the events of temperature adaptation in the newborn.

BODY TEMPERATURE DURING NEONATAL PERIOD

The body temperature of the newborn infant falls rapidly[1–4] in the usual environmental conditions of the delivery room and nursery. The rate of fall of deep body and skin temperatures in the immediate neonatal period approximates 0.06 and 0.17° F. (0.1 and 0.3° C.) per minute, respectively.[4] The average fall in rectal temperature during the first one to two hours in healthy term infants approximates 3° F. (1.8° C), and rectal temperatures of 94 to 95° F. (34.4 to 35° C.) are not uncommon at 2 to 4 hours of age.[1–3] However, most term infants are capable of adequate defense against this precipitate cold stress, and rectal temperatures increase to relatively normal levels by 8 to 24 hours of age.[2,3] On the other hand, body temperature in premature infants is more labile, and the early neonatal fall in temperature may be considerably greater than in term infants. In addition, the return to more normal body temperature may be considerably delayed. Most small premature infants are unable to achieve normal body temperature without exogenous support.[3,5] Recent investigations have shown a significantly increased mortality in premature infants kept at relatively low environmental temperatures.[6–10] Results of several of these studies are summarized in the table.

RESPONSES TO ENVIRONMENTAL COLD STRESS

It is clear, then, that one of the most profound initial challenges to the newborn infant relates to the maintenance and stabilization of body temperature in the relatively cold extrauterine environment. For this task, the infant appears to be equipped with the full spectrum of cold defense mechanisms characteristic of homoiothermic species, as well as the capacity to program these responses in order to overcome his inherent disadvantages. Only in the small premature infant do these mechanisms fall short of homoiothermy.

The responses to cold stress in homoiothermic species, including the human neonate, include [1] fluid volume changes and water diuresis, [2] reduction of environmental heat exchange (peripheral vasoconstriction or decrease in evaporative water loss), and [3] increase in metabolic heat production (shivering or nonshivering).

FLUID VOLUME CHANGES AND WATER DIURESIS

Acute cold stress in animals and man produces a decrease in plasma volume accompanied by hemoconcentration.[11] Although available data are somewhat conflicting, it would appear that the predominant proportion of the displaced plasma volume remains extracellular.[11] The duration of this effect is short; with prolonged cold exposure (several days), changes in plasma and blood volume, hematocrit, serum protein concentration, or extracellular water volume are not observed.[11] Acute cold exposure also provokes a water diuresis which occurs without associated

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D. A. FISHER *is associate professor, Department of Pediatrics, University of Arkansas Medical School, and* E. J. MAKOSKI *is a medical student, University of Arkansas Medical School, Little Rock.*

change in glomerular filtration rate or renal plasma flow and can be prevented by vasopressin (Pitressin®) administration.[11,12] This "cold diuresis" differs from the usual water diuresis in that a concomitant increase in sodium and chloride excretion is observed.

These effects on water metabolism have been observed in newborn infants during the first hours and days of extrauterine exposure. A marked increase in hematocrit and decrease in plasma volume have been reported in the neonate during the first three to four hours of life.[13-17] This hemoconcentration in the newborn has been shown to be a response to extrauterine cooling.[17]

The rise in hematocrit may exceed 10% within fifteen minutes of birth and may exceed 25% by 3 to 4 hours of age.[13] A concomitant but lesser increase in concentration of serum protein is observed without change in serum sodium concentration.[13] The lack of change in sodium concentration and an observed tendency to acute increase in limb volume in the neonate during the first few hours[14] are compatible with the assumption that the plasma is displaced to the interstitial fluid compartment. As is the case in adults, this hemoconcentration is transient and largely disappears by twenty-four hours.[14]

Significantly larger urine volumes have been observed in the neonate exposed to relatively low environmental temperature in contrast to those kept in near-neutral thermal environments.[17,18] This increased urine volume appears to be a water diuresis because urine osmolality in the hypothermic infants is significantly lower than that of incubated infants.[17] Moreover, solute excretion and endogenous creatinine clearance are similar in the 2 groups of infants.[17] This water diuresis in the hypothermic infant is insignificant during the first twelve hours and becomes progressively more pronounced during the subsequent thirty-six hours.[17]

The mechanism and significance of the plasma volume change with acute cold exposure are not understood. The decrease in plasma volume can be prevented by brainstem transection immediately posterior to the mammillary bodies, suggesting a hypothalamic mediation.[11,19] Moreover, it occurs in spite of prevention of the water diuresis with Pitressin®[11] and in the newborn infant occurs before obvious water diuresis.[17] This decrease in plasma volume is due, presumably, to increased capillary hydrostatic pressure during the early minutes of life. Increased central venous pressure has been reported in the newborn during the early neonatal period, and the time course of falling venous pressure during the first few hours of life seems to parallel that of falling plasma volume.[14,20,21]

There is considerable evidence supporting the hypothesis that the osmotic pressure of body fluids is one of the mechanisms regulating evaporative water loss.[11,22-26] Salt loading in animals and man has been shown to decrease insensible perspiration[11,22-24] and in infants to impair tolerance to high environmental temperature.[24] Dehydration in children decreases and overhydration increases insensible water loss without alteration in total heat loss.[25,26] The explanation of the effect of osmotic pressure on evaporative water loss is obscure. It may represent a simple process of physical diffusion whereby the increase in osmotic pressure decreases the available water for vaporization, or it may be the result of alteration of the subthreshold activity of sweat glands.[23]

Barbour has suggested that the cold-induced plasma volume displacement is a primary response oriented to decreasing evaporative water loss by reducing cellular osmotic pressure. He based this suggestion on his belief that the plasma water was displaced intracellularly,[19,22] which is probably not the case.[11] Decrease in plasma volume with hemoconcentration and increase in interstitial volume without change in body water osmolality would not be expected to alter significantly the osmolality of skin and subcutaneous water so that vaporization would be inhibited. Others have speculated that the hemoconcentration most likely represents a nonspecific effect of more primary cold defense mechanisms.[11,27,28] The present authors are inclined to this view also. The association of the decrease in plasma volume with progressively decreasing central venous pressure in the early neonatal period suggests that this phenomenon is related to early peripheral vasoconstriction and venoconstriction, perhaps mediated reflexly by the nervous system or by the temperature-induced increase in catecholamine secretion.

The water diuresis in the cold-exposed newborn is due, at least in part, to a relatively greater fluid and caloric intake by these infants.[17] However, the similarity of calculated nonrenal water metabolism in cold and warm infants[17] suggests that the water diuresis in cold infants may not be primarily related to a greater metabolic rate and, consequently, greater fluid intake. The possibility of a "cold diuresis" similar to that in the acutely cold-exposed adult,[12] and perhaps secondary to cold-induced antidiuretic hormone inhibition, requires further investigation.

The possible significance of such a cold-induced water diuresis to cold defense is ob-

TEMPERATURE AND SURVIVAL OF PREMATURE INFANTS

	Number of infants		*Ambient temperature (° C.)*		*Survival (percent)*		*Weight range (gm.)*
	Control	*Study*	*Control*	*Study*	*Control*	*Study*	*Same for both control and study*
Silverman and associates 1958[7]	91	91	28.3 to 29.4	31.1 to 32.2	68.1	83.5	1,001 to 1,501+
Jolly and associates 1962[8]	97	104	29.4	35.6 to 37.2	57.4	70.6	1,000 to 2,500
Buetow and Klein 1964[9]	69	89	31.1 to 32.2	36 ± 0.2	46.5	58.4	1,000 to 1,500
Day and associates 1964[10]	41	46	31.8	incubated*	63	77	600 to 1,999

*Skin thermistor temperature set to 36° C.

scure. It has been speculated, in the adult, to be a mechanism for decreasing evaporative water and heat loss by way of increasing the osmotic pressure of body fluids.[11] The data of Day and colleagues[10] in infants and quoted adult data do not show a convincing decrease in absolute or proportional evaporative heat loss with cooling below 30° C. Whether significant reduction in evaporative water loss occurs with cooling and whether this might be influenced by the water diuresis in adults or in the newborn, therefore, remain speculative.

REDUCTION OF ENVIRONMENTAL HEAT EXCHANGE

Peripheral vasoconstriction. This has been shown to occur in the newborn infant in response to exposure to low ambient temperature.[5,29] Brück[29] has demonstrated that cooling to 23 to 28° C. produces maximal constriction of skin vessels. Day and associates[5] have shown that heat loss by radiation and conduction over a range of ambient temperature of 26 to 34° C. is similar on a square meter surface area basis in premature infants and adults; since loss of heat by these routes is dependent on skin temperature, which in turn is related to skin blood flow, it was concluded by these investigators that the peripheral vascular responses of infants over this range of ambient temperature were comparable to those of adults. In addition, the efficiency of circulatory reactions of premature infants was compared to that of adults in terms of thermal conductivity, defined as the total heat loss per hour per square meter body surface per degree centigrade of difference between body core and skin temperature.[5] Again, mean values were similar to those of the adult over the range of skin temperature of 33 to 37° C.

Regulation of evaporative water loss. Day and associates,[10] in studies of infants, has shown that evaporative heat loss remains approximately 30% of total heat loss with decreasing air temperature from 30 to 27° C. Absolute values for evaporative heat loss over this temperature range were about 10 to 15 calories per square meter per day. With increasing air temperature to 34° C., the infants, in general, did not increase absolute evaporative heat loss although losses through radiation and convection decreased. Proportionate evaporative loss, therefore, increased to about 50%. At high air temperature most infants, in contrast to adults, showed little visible sweating (relative humidity was usually 50 to 60%).[10] Thus, in small infants, little or no effective regulation of evaporative waterloss is observed. The major routes of heat loss are radiation and convection, which account for perhaps 80 to 50% of total heat loss over a range of environmental temperature of 27 to 33° C.

Total heat loss per square meter surface area at low ambient temperature in newborn term and premature infants is known to be greater than that of adults.[5] Although this is due, in part, to the infant's greater heat production, heat loss in proportion to heat production is also greater than in the adult. This excessive heat loss is due to the higher skin temperature in infants at all environmental temperatures between 26 and 34° C.[5] and to the greater thermal conductivity of the infant in contrast to the adult. The latter derives from inherent physical characteristics of infants—the relatively greater surface area to body mass ratio, smaller body shell, and thinner layer of subcutaneous fat[5,29,30]—for which the only defense is an increased rate of heat production.

INCREASE IN METABOLIC HEAT PRODUCTION

Shivering. Adequate quantitative data regarding the relative contributions of shivering and nonshivering thermogenesis to total metabolic heat production in infants exposed to cold are also meager. Activity of normal term infants in a cool environment is increased. Such infants are more irritable and restless, and they exhibit more crying and fretfulness. The proportion of time they spend sleeping is less than for infants in a more neutral thermal environment.[5,29–32] Available data would suggest, however, that, in contrast to adults, increased muscular activity is not the predominant source of increased heat production in the neonate during acute cold stress.

Brück[30] has shown in guinea pigs that even the increased oxygen consumption associated with maximal muscular activity in cold-exposed adult animals would supply only about half of that necessary to compensate for the relatively large heat loss in the newborn exposed to similar environmental conditions. The muscular activity in the newborn infant, often less than visible shivering, would contribute considerably less. In premature infants, visible shivering with acute cold exposure has been reported to occur less frequently than in term infants. It is thought that their greater thermal instability in the cold is due, in addition to inherently greater thermal conductivity, to decreased shivering.[29,33–35]

Nonshivering thermogenesis. This is the predominant defense against hypothermia in premature as well as term newborns.[29–41] Oxygen consumption increases strikingly during the early hours of postnatal life to reach plateau levels by about seventy-two hours.[29,36,41] Acute cold exposure provokes further increments in oxygen consumption in premature and term neonates.[29,31,32,35,37,39] This acute cold responsiveness, which can be minimized by exposure to a low oxygen atmosphere,[36,42,43] also appears to increase in magnitude during the first several days of life.[29] Highest values for oxygen consumption in response to cold exposure compare favorably with those reported for adult man under maximal cold stress.[29,32] Adamsons and colleagues[32] have shown that oxygen consumption in the neonate shows an inverse linear correlation ($r = 0.906$) with environmental temperature over the range of ambient air temperatures of 12 to 40° C. The cold-induced increase in oxygen consumption in their study correlated best with the temperature gradient between the skin and the environment, suggesting that acute cold-induced thermogenesis is mediated by thermal skin receptors.[32]

Adams and associates[41] have interpreted data from their study of premature infants at ambient temperatures of 32 to 34° C. as demonstrating a temperature coefficient effect, that is, a reduction in metabolism secondary to a lowered body temperature. The temperature coefficient effect was not observed in these same infants at ambient temperatures above or below 32 to 34° C.[41] and has not been observed in other studies.[29,32,39]

Respiratory quotients appear to be quite low in the neonate and quite variable. Values tend to decrease over the first three days and subsequently increase to more normal values.[29,36,41] Individual respiratory quotient responses to cooling are quite variable but, in general, mean values tend to change little.[35] The extremely low respiratory quotient values of the neonate, often as low as 0.7, may reflect factors other than the rate of carbon dioxide production;[35,36] the possibility of extrapulmonary carbon dioxide exchange, the presence of acidosis, the unsteady state due to increased muscle tone and movement, and technical problems of measurement all may introduce significant error. However, the residual low values with cooling do suggest low carbon dioxide production and fatty acid rather than glucose utilization.[35]

Studies in newborn rabbits have shown increased plasma glycerol and free fatty acid levels in response to cold exposure indicating breakdown of adipose tissue triglyceride.[44] Similar increases in glycerol and free fatty acid have been reported in the newborn infant at usual nursery temperatures, suggesting a similar cold-induced lipid mobilization.[45–48] This mobilized lipid probably serves an important substrate role in neonatal thermogenesis since a concomitant increase in serum ketone levels also occurs and since administration of glucose will suppress the increase in free fatty acid and the concomitant rise in serum ketone levels.[48] Moreover, free fatty acid has been shown to increase in vitro oxygen consumption of diaphragms from animals up to about fourteen days of age in further support of the suggestion that fat and free fatty acid play an important role in the cold thermogenesis of the newborn.[49]

Dawkins and Hull[44] have shown that adipose tissue, in addition to providing substrate for increased nonadipose tissue thermogenesis, appears to provide a highly exothermic cycle of norepinephrine-stimulated hydrolysis and resynthesis of triglyceride within the adipose tissue cell. This local thermogenic process is present in both white and brown adipose tissue but is apparently more active in the latter. Smith[50] has suggested that this high metabolic activity of brown fat, its relative abundance in the newborn of several species, and its localization to perivascular areas and areas of confluence of afferent vessels from the periphery may indicate a unique role for this tissue as a thermogenic jacket for vascular return from the periphery. Silverman and colleagues[51] have demonstrated that during cold exposure of the newborn infant the nape of the neck remains relatively warm in agreement with Smith's proposal.

ENDOCRINE RESPONSES

Catecholamines. Increased catecholamine and, more particularly, norepinephrine secretion have been demonstrated with acute cold exposure and chronic cold acclimation in animals.[52–54] Moreover, this increase in catecholamine secretion appears to be essential for the thermogenic response to cold exposure; adrenergic blockade inhibits or abolishes the increase in oxygen consumption and increases mortality with cold exposure in animals without altering the response to exogenous norepinephrine.[49,53–55] In newborn animals, norepinephrine infusion, similar to cold exposure, has been shown to promptly increase oxygen consumption and carbon dioxide production, to mobilize lipid stores, and to increase plasma glycerol and free fatty acid levels in association with an increase in body temperature.[44,49,54,55] Therefore, it is generally accepted that catecholamines play a major role in the mediation of cold thermogenesis, more particularly norepinephrine released from postganglionic sympathetic nerve endings during sympathetic nervous system activity.[49]

In the newborn infant, increase in catecholamine excretion in response to cold exposure and in association with acute increase in oxygen consumption has been demonstrated.[18,56] In addition, an increased sensitivity of the neonate to exogenous norepinephrine thermogenesis has been described.[49,57–59] This effect is similar to the enhanced thermogenic response to exogenous norepinephrine characteristic of cold acclimated animals.[49,54] In the newborn, however, the norepinephrine sensitivity is transient and disappears after the first few weeks of life.[57,58] The increased catecholamine excretion and plasma free fatty acid levels[18,46,56] with cold exposure and the prompt increase in oxygen consumption and in plasma free fatty acid concentrations during norepinephrine infusions[59] have suggested that norepinephrine is a major mediator of nonshivering thermogenesis in the newborn infant, as had been suggested earlier by Moore and Underwood[60] in newborn small animals.

Thyroid hormone. During the first few days of extrauterine life, serum hormonal iodine values increase markedly.[2,17,61–66] Thyroid hormone binding protein concentrations remain unchanged, however,[66] and increased saturation of binding proteins occurs, I^{131}-labeled triiodothyronine erythrocyte[67,68] and resin uptake values[64] are elevated, and free thyroxine titers presumably increase. Thyroidal radioiodine clearance is also high during this early neonatal period.[2,17,64] Investigations in nonincubated and in incubated infants have shown that the increments in protein-bound iodine and thyroidal radioiodine clearance characteristic of the first forty-eight hours of life are significantly less in incubated infants.[17,64] The association of high protein-bound iodine values with high thyroidal radioiodine clearance in hypothermic infants, in contrast to lower values in incubated infants, indicates failure of the usual feedback suppression of thyrotropic hormone secretion in the cold infants and suggests a direct stimulation of thyrotropic hormone secretion by the exposure to the cool extrauterine environment.[17]

The role of thyroid hormones in cold exposure has not been defined completely. Thyroxine has been shown to potentiate the thermogenic effect of catecholamine;[69,70] oxygen consumption in response to epinephrine in thyroidectomized rats increases in proportion to the log dose of thyroxine.[69] The increased sensitivity of the neonate to norepinephrine thermogenesis during the first month of life[49,57–59] correlates temporally with the period of increased serum hormonal iodine[63,64] and presumably represents thyroid hormone potentiation of chemical thermogenesis. The progressive increase in oxygen consumption in response to acute cold exposure during the first few hours and days of life,[29] during which time serum hormonal iodine values are progressively increasing,[64] is in agreement with such an interpretation.

Thyroid hormones have also been shown to serve a specific and requisite role in mobilization of fatty acid from body fat stores in response to catecholamine.[71,72] It would appear, then, that thyroid hormones serve a dual role in the defense against cold exposure; they serve an essential role in substrate mobilization as well as a potentiating role in the consequent thermogenic response.

Adrenal corticosteroids. The hormonal response to cold exposure in animals has been shown to include increased adrenal corticosteroid secretion.[73–75] This effect is variable, however, and appears to depend upon the magnitude of the cold stimulus and the nutritional state of the animal as well as species differences.[74,75] Ulstrom and colleagues,[76] measuring methylene chloride extractable plasma 17-hydroxycorticosteroids in nonincubated term newborns, reported suggestively elevated values in pooled venous samples between three and twelve hours of life as contrasted with values in pooled cord blood or later twelve-hour plasma pools. Kenny and associates[77] were unable to demonstrate significant variation in daily cortisol secretion rates in normal nonincubated newborns during the first two weeks of life, and, more recently, Hillman and Giroud[78] have reported a significant decrease in plasma cortisol and cortisone in nonincubated term infants during the first twenty-four hours of life.

Fisher and Oddie[17] noted no differences in excretion rates of urinary methylene chloride extractable 17-hydroxycorticosteroids in incubated and nonincubated term infants during the first forty-eight hours. However, since many of the adrenal cortical secretory products characteristic of the neonatal period would not be extracted and/or measured by the methylene chloride–Porter-Silber technique, this data does not completely exclude a possible role of the adrenal cortex in neonatal cold stress.

Antidiuretic hormone. The significantly larger urine volume[17,18] of low osmolality[17] in cold-exposed as contrasted with incubated infants resembles the water diuresis observed in cold-exposed adults. The latter occurs without change in glomerular filtration rate or renal plasma flow and can be prevented by Pitressin® administration.[12] Such cold diuresis is thought to result from inhibition of antidiuretic hormone release, although this has not been confirmed by direct analyses for antidiuretic activity of plasma or urine in cold-exposed animals or in man; acute heat stress has been shown to provoke a discharge of antidiuretic hormone in the rat.[79]

NEURAL CONTROL OF TEMPERATURE RESPONSES

The redistribution of plasma water appears to be stimulated by the hypothalamus,[19] perhaps by way of the increased catecholamine secretion. Peripheral vascular adaptations to cold exposure are thought to be regulated predominantly by reflexes from receptors in the skin. However, activation of central receptors cannot be excluded. Such receptors in animals have been shown to be responsive to changes in blood temperature of about 0.2° C.[80] The mode of control of shivering is defined less well, but available evidence would suggest that this response is mediated also by thermal receptors in the skin as well as by central receptors, probably in the hypothalamus.[80]

Adamsons and colleagues[32] have shown that the increase in oxygen consumption in the neonate in response to cold exposure occurs within minutes and is stimulated by thermal receptors in the skin. Data of Brück[30] would suggest that the sensitivity of these thermal skin receptors in the newborn may be greater than in the adult; increases in oxygen consumption in the newborn in response to cold exposure occur at higher ambient temperatures, and the rate of increase with decreasing ambient temperature is greater than in the cold-exposed adult. Since the response to exogenous norepinephrine in the newborn is temporally similar[59] to the response to cold, it seems likely that the cold-induced increase in oxygen consumption is catecholamine mediated. It would follow that the stimulation of catecholamine secretion is also mediated by peripheral (skin) thermal receptors.

In animals, stimulation of thyroid function in response to cold exposure has been shown to occur reflexly by way of the hypothalamus and pituitary; pituitary stalk section, anterior hypothalamic lesions, or median eminence lesions will prevent such stimulation.[81–83] This thyroid stimulation is elicited predominantly by increased neural inflow from peripheral cold receptors, although possible influence by hypothalamic temperature receptors may occur.[83] Although the mechanism of the cold stimulation of thyrotropic hormone release in the newborn is not known, analogy with the cited animal data would suggest predominant peripheral thermal receptor stimulation. Since hypothalamic temperature has been shown to correlate with deep rectal temperature in circumstances of stable thermal environment in animals[84] and since infants with detectable thyroid stimulation are usually hypothermic before the time the thyroid stimulation is observed,[17] the possibility of central receptor mediation of the thyroidal hyperactivity cannot be excluded.

SUMMARY

The newborn infant, because of a larger surface area to body mass ratio, a smaller body shell, and a thinner layer of subcutaneous fat, has a greater thermal conductivity than does the adult. As a result, his rate of heat loss by way of conduction and radiation in a cool environment is much greater than is that of the adult. His precipitate transfer from the 37° C. intrauterine environment to the relatively cool environment of the delivery room and nursery results in a fall of deep body and skin temperatures, which in the immediate neonatal period may approximate 0.1 and 0.3° C. per minute, respectively. Defense against this abrupt hypothermia, probably mediated by way of thermal skin receptors and integrated through the hypothalamus, is rapidly mobilized and includes peripheral vasoconstriction, comparable in degree to that in adults, significant increase in activity, and, occasionally, frank shivering, particularly in term infants.

Increased sympathetic nervous system activity and the resultant increased secretion of catecholamines, probably stimulated by skin receptors, enhance peripheral vasoconstriction and venoconstriction and probably increase capillary hydrostatic pressure, with a resulting shift of plasma to the interstitial fluid compartment. More importantly, norepinephrine stimulates a marked increase in metabolic rate, manifest by nearly proportionate increases in oxygen consumption and carbon dioxide production.

Stimulation of thyrotropic hormone release produces a marked increase in thyroid hormone secretion, resulting in increased serum hormonal iodine levels, increased saturation of thyroxine-binding proteins, and increased thyroidal radioiodine uptake. The increased thyroid hormone secretion enhances the thermogenic effects of catecholamines, probably accounting for the progressive increase in oxygen consumption with age and the increased sensitivity to exogenous norepinephrine thermogenesis characteristic of the newborn during the first few days and weeks of life, respectively.

The increased metabolic rate, stimulated by norepinephrine, enhanced by thyroid hormones, and probably sustained largely by fat stores, effectively increases heat production. Skin temperature increases in spite of the vasoconstriction, since the thermal conductivity is high, and heat loss increases. In most infants, except the small premature, the increased heat production is adequate, in spite of the increased heat loss, to reverse the falling body temperature by 3 to 4 hours of age, and a progressive increase in body temperature is observed. Thermogenesis is regulated thereafter to balance heat production against the relatively high rate of heat loss.

A cold-stimulated water diuresis also occurs in the newborn at low ambient temperatures, but the mechanism and significance are not at present understood. Adrenal corticosteroid secretion does not appear to be significantly influenced in the newborn by usually encountered environmental temperatures.

Nonshivering thermogenesis in the neonate occurs at higher ambient temperature than in adults. The adult also achieves homoiothermy without the need for the excessive thyroidal stimulation seen in the newborn; little or no increase in protein-bound iodine is seen in adults exposed to moderate cold. These differences can be explained by the relatively high thermal conductivity and consequent high rates of heat loss in the newborn infant. Practical considerations regarding management during the neonatal period have been discussed recently by Oliver.[85]

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Congenital Coronary Artery Fistula

Communication of the Left Coronary Artery with the Left Atrium

FLORENCE CHAR, M.D., and MASAUKI HARA, M.D.

Little Rock, Arkansas

SINCE THE DEVELOPMENT of retrograde aortography and improved cardiac catheterization techniques, there has been an increasing number of reports on congenital coronary artery fistulas. Recent reviews on the subject[1–12] attest to the increasing frequency of recognition of the anomaly and the feasibility of total surgical correction. To date, more than 90 cases of coronary artery fistula have been reported in the literature; approximately one-third of these were successfully corrected by surgery.

Coronary fistulas of various anatomic types have been described. Such fistulas have been reported communicating with the right atrium, right ventricle, coronary sinus, great cardiac vein, left superior vena cava, pulmonary artery, left ventricle, and left atrium. Approximately 90% of the reported cases are of fistulous channels emptying into the right side of the heart. Communication of a coronary artery with the left heart is relatively rare. Only 3 cases of isolated coronary-left atrial fistula have been reported.[9,13,14] Two of the 3 were diagnosed at surgery.[13,14] Details of the third case were unknown. A fourth case, described by Heiner and associates,[15] probably represents an aortic sinus aneurysm rather than an anomalous left coronary communication with the left atrium. A fifth case recently reported by Sloman and associates[16] consisted of a left coronary fistula communicating with the left atrium and pulmonary artery.

The purpose of this paper is to report a case of left coronary artery–left atrial fistula, diagnosed preoperatively and successfully corrected.

CASE REPORT

An almost 5-year-old Caucasian girl was first examined in the University of Arkansas Medical Center pediatric cardiology clinic in the fall of 1963 because of a heart murmur known since birth. The patient had been in relative good health except for a bout of pneumonia at age four months; at that time her parents were told by her physician that there was a "hole in the heart." There was no history of congestive heart failure and no cyanosis. The patient had mild decrease in exercise tolerance as compared to other children and frequently complained of nonspecific abdominal pains.

The prenatal history and birth history were normal. The birth weight was 6 lb. 8 oz.; growth and development were normal. The family history was noncontributory except for the patient's father who died at age 47 because of rheumatic heart disease, aortic stenosis, and aortic insufficiency.

Physical examination. Height was 112 cm. and weight was 20 kg. Pulse rate was 110 per minute and the respiratory rate was 20 per minute. Blood pressure in the right arm was 120/70 mm. Hg and in the leg was 130/70 mm. Hg. There was no evidence of cyanosis. A prominent thrill was felt best over the anterior axillary line and fourth left intercostal space. A grade III continuous, machinery-type murmur was heard best in the third to fourth left intercostal space and the anterior axillary line (Fig. 1). The intensity of the murmur did not vary appreciably with respirations. The murmur was poorly transmitted to the posterior lung field. The remainder of the physical examination was not remarkable.

Electrocardiogram. The electrocardiogram (Fig. 2) revealed a rate of 110 per minute, normal axis deviation, PR interval of 0.14 seconds, and tall R waves in left precordial leads. The vectorcardiogram revealed a counter-clockwise loop in the horizontal plane. The loop was somewhat displaced posteriorly suggestive of left ventricular preponderance.

Roentgenograms. The posteroanterior view of the chest (Fig. 3) revealed a prominent aortic knob and an irregular left cardiac border near the position of the left atrial appendage. The pulmonary vasculature appeared to be normal. The left atrium and left ventricle appeared slightly enlarged.

First University of Arkansas Medical Center admission was in October 1963. Cardiac catheterization studies revealed the following data:

FLORENCE CHAR *is assistant professor, Department of Pediatrics, University of Arkansas Medical Center, and* MASAUKI HARA *is professor, Department of Surgery, University of Arkansas Medical Center, Little Rock.*

	Oxygen saturation (%)*	*Pressure mm. Hg*	
Inferior vena cava	69.6		
Superior vena cava	66.8		
Right atrium	69		mean 3
Right ventricle	69	42/0	
Pulmonary artery	69.1	40/9	mean 25
Pulmonary capillary			mean 11
Femoral artery	93	133/72	mean 98

*O_2 saturation figures are average of several samples.

Since the right heart catheterization did not reveal evidence of a shunt, a retrograde aortogram was then attempted from the right brachial artery. A No. V Rodriguez-Alvarez catheter was placed into the ascending aorta in the region presumed to be above the aortic valve (Fig. 4). While awaiting injection of the contrast media the patient was suddenly noted to be pale and unresponsive. The monitoring electrocardiogram revealed evidence of marked bradycardia and ST-T changes (Fig. 5). Immediately the catheter was pulled back several inches and external cardiac massage was instituted. Within moments the electrocardiogram reverted to sinus rhythm. The patient became responsive and apparently showed no ill effect. In view of this episode, it was elected to defer the contemplated studies.

Second admission was in October 1964. A retrograde aortogram was performed with injection of 80% sodium iothalamate into the ascending aorta without event. A large fistulous tract from the aorta into the left atrium was demonstrated (Fig. 6).

The patient was readmitted in June 1965 for surgical correction of the defect.

Operative findings. The left coronary artery was markedly enlarged to a diameter of about 1.2 cm. with thinning of the wall. A saccular aneurysm measuring 3 cm. in length, 2 cm. in width, and 1.8 cm. in height was present in the vessel 3.5 cm. from its origin at a site medial and anterior to the base of the left auricle. The coronary artery distal to the aneurysm was also enlarged. A continuous thrill was palpated in the aneurysm which could be obliterated by pressure in a localized, slightly depressed area near the atrioventricular junction. Exploration of the left atrium through the appendage revealed a definite fullness, seemingly like a mass, in the wall above the middle one-third of the anterior mitral leaflet, but a thrill could not be felt. The slit-like fistula measured 1 mm. wide and 4 to 5 mm. long in the posterior wall of the coronary artery, emptying into the left atrium. The right coronary artery was moderately enlarged with a sizable branch traversing the right ventricular outflow region to inosculate with a small left anterior descending coronary artery. The ascending aorta was enlarged to a diameter of 2.5 cm.; the main pulmonary artery was considerably smaller, measuring about 1.6 cm. in width (Fig. 7).

Operative procedure. The heart was exposed through a midline sternotomy incision. After exploration of the exterior of the heart had been carried out, the aneurysm and the adjacent proximal coronary artery were dissected free. The site and origin of the fistula was identified as lying embedded in the myocardium. Although the fistula was partly isolated, it was considered safer to close the fistula from within the lumen of the artery using cardiopulmonary bypass. Accordingly, extracorporeal perfusion was instituted and the patient's temperature was rapidly lowered to 33° C. The aorta was cross-clamped for three minutes while the aneurysm was opened and the fistula closed with two figure-of-eight dacron sutures. A small Satinsky type of vascular clamp was applied to the base of the aneurysmal sac which was obliterated with two rows of continuous 5-0 arterial sutures. The heart was defibrillated with a single direct current shock and restored to a sinus rhythm. The thrill had disappeared and the left coronary artery appeared less distended. The postoperative course of the patient was uneventful except for a fever of 100 to 101° F. during the first five days. The murmur had disappeared and she was discharged on the eighth postoperative day.

COMMENT

Coronary artery fistulas into a cardiac chamber or pulmonary artery without other associated defects in the pediatric age group usually are

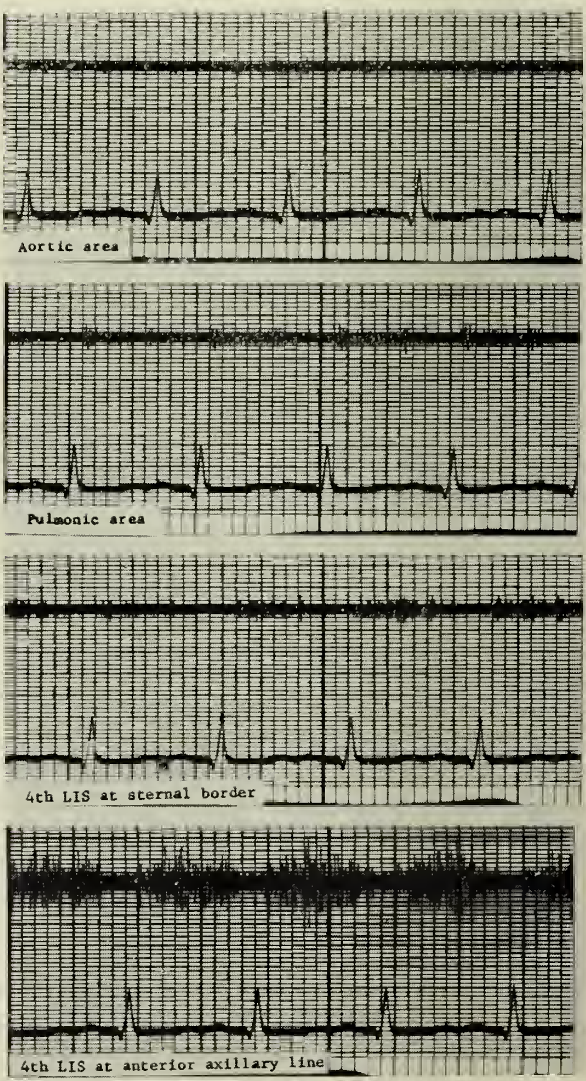


Fig. 1. Preoperative phonocardiogram demonstrating continuous murmur at the fourth left intercostal space and anterior axillary line

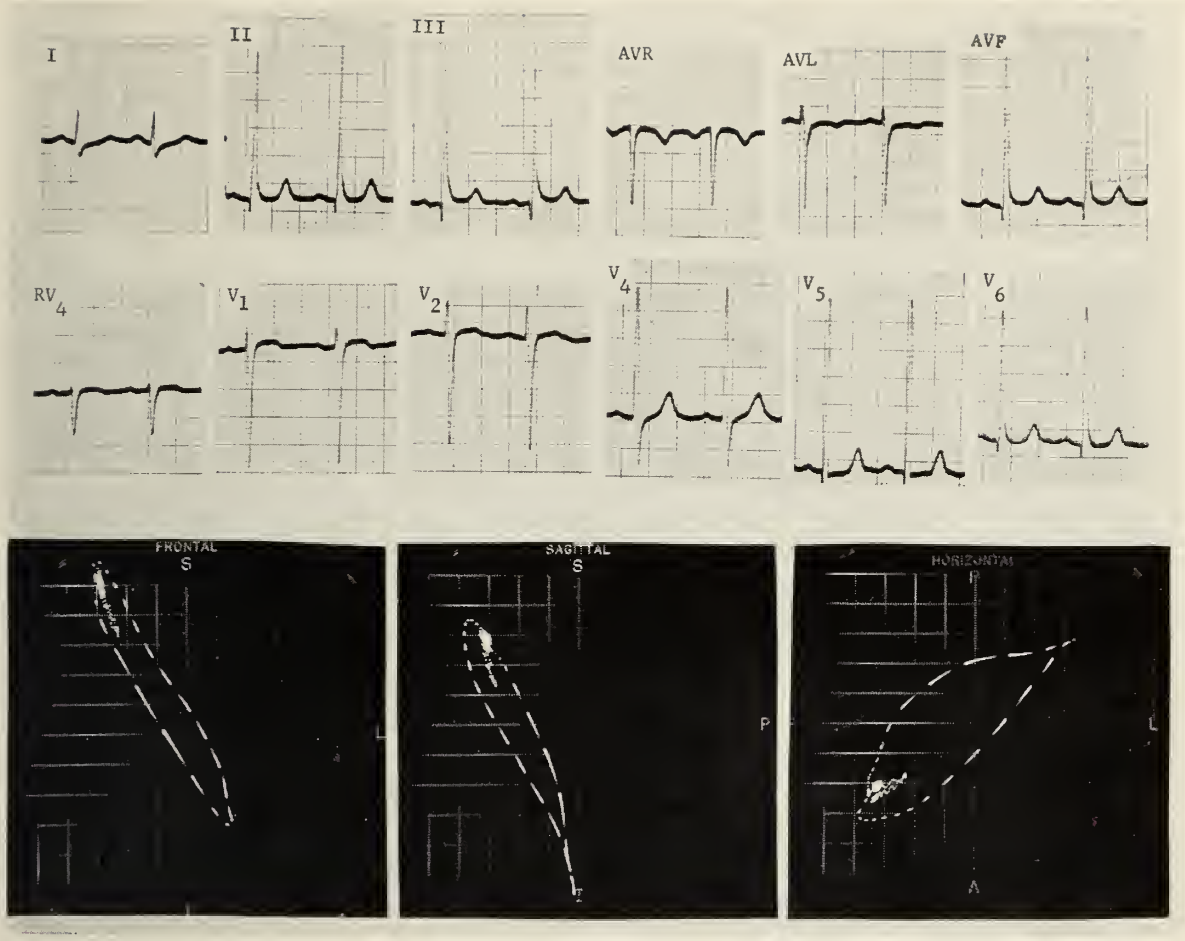


Fig. 2. Electrocardiogram and vectorcardiogram (Frank system) demonstrating left ventricular preponderance

relatively asymptomatic.[9,17,18] However, the degree of symptomatology depends upon the location of the fistula and the size of the shunt. The size and length of the fistula are probably the two most important factors. In the case described, the coronary artery was not tortuous but there was a saccular aneurysm and the entry into the left atrium was relatively small. Hemodynamically the amount of aortic-left atrial flow was probably not torrential but definitely significant as demonstrated by the elevation in the pulmonary wedge pressure and left atrial and ventricular hypertrophy.

Myocardial ischemia associated with congenital coronary artery fistula has been described.[6,12,19,20] Electrocardiographic changes are dependent upon the alterations in hemodynamics. In the case presented, evidence of left ventricular hypertrophy was present. No definite evidence of myocardial ischemia was found, even though the myocardium was predominately supplied by the large right coronary artery. One may speculate that the marked ischemic episode

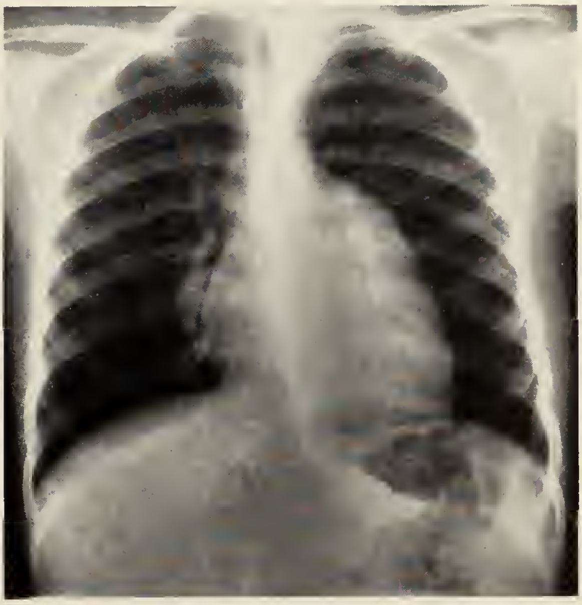


Fig. 3. Roentgenogram of chest in the posteroanterior view showing normal pulmonary vasculature and prominent left heart border

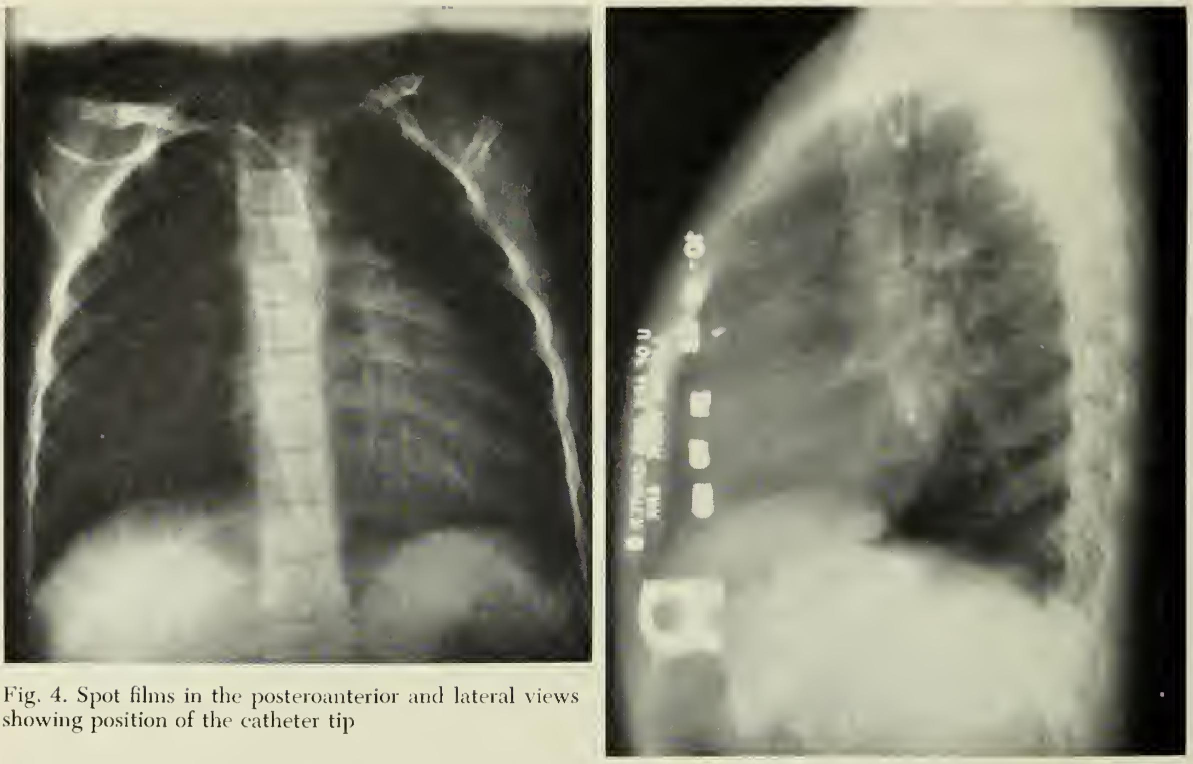


Fig. 4. Spot films in the posteroanterior and lateral views showing position of the catheter tip

at the first attempt at angiocardiography represents occlusion of the right coronary artery by the tip of the catheter. In retrospect, the tip of the catheter was at the site of the right coronary ostium. (Compare Figs. 4 and 3-6.) It may be justified to emphasize the need to prevent such a catastrophe in the performance of aortography by not placing the catheter tip too close to the aortic root so as to occlude a coronary ostium, especially when a coronary artery fistula or a single coronary artery is suspected. Continuous recording of the aortic pressure is also a helpful guide to assess the position of the catheter tip.

Abbott and associates[2] summarized the surgical treatment and results of the arteriovenous fistulas reported to 1961. Of the 27 patients operated upon, 10 had ligation of the involved coronary artery with 2 having, in addition, transaneurysmal ligation of the fistula. Ligation of the aberrant artery was accomplished in 8, ligation of the fistula in 3, and endo-aneurysmorrhaphy in 1. Unspecified procedures were performed in 3 other cases. Several other cases[1,3–7,21,22] have been recorded in the literature since the study of Abbott. Ligation of the fistula has increasingly become the preferred treatment. Cooley[22] has recommended closure of the fistula and cautioned against ligation of a large coronary artery proximal and distal to the fistula because of the development of complications due to ischemia of the myocardium in two of his patients, both of whom recovered. The fistula in the patient described herein could have been isolated and ligated, but, in view of the relative inaccessibility of the fistulous tract and the thin vein-like quality of the coronary artery, it was decided to close the fistulous opening from within the aneurysm.

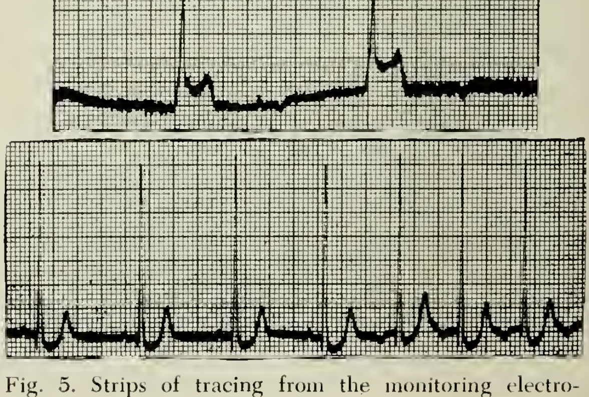


Fig. 5. Strips of tracing from the monitoring electrocardiogram during the ischemic episode

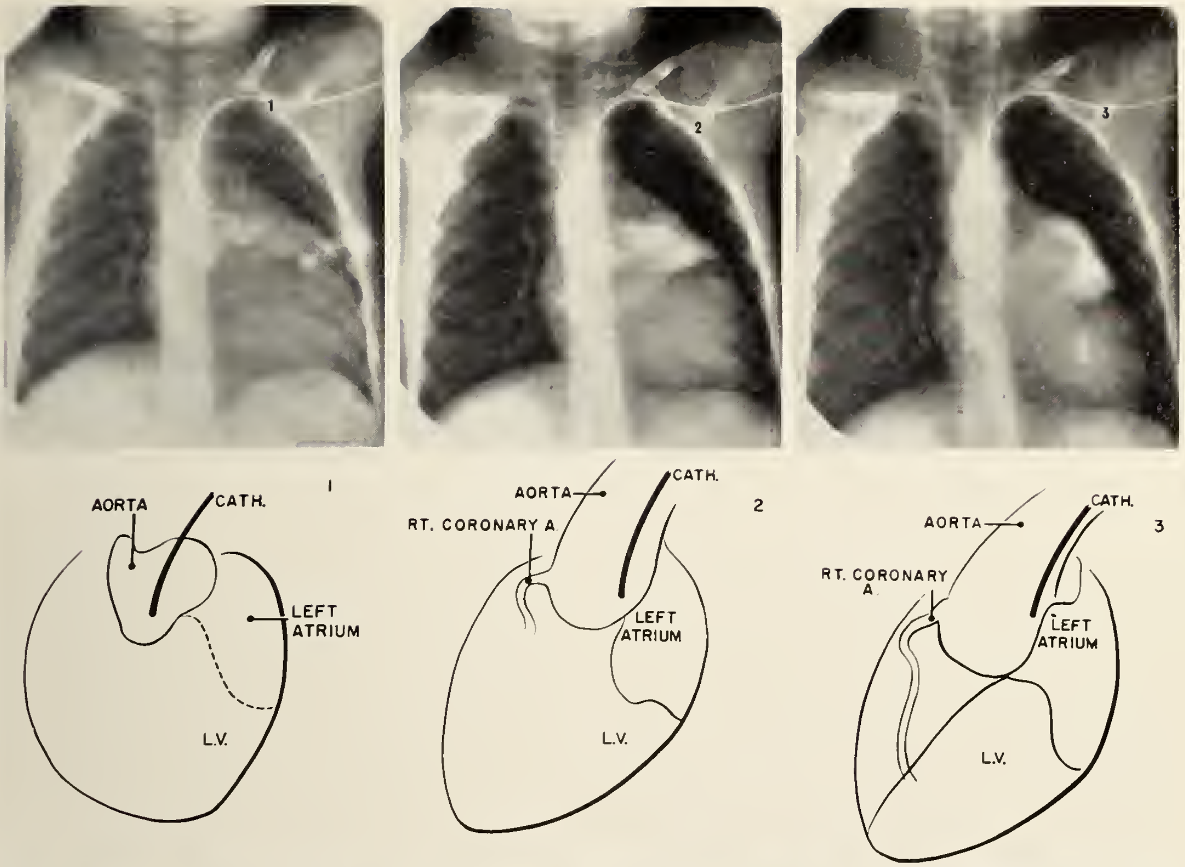
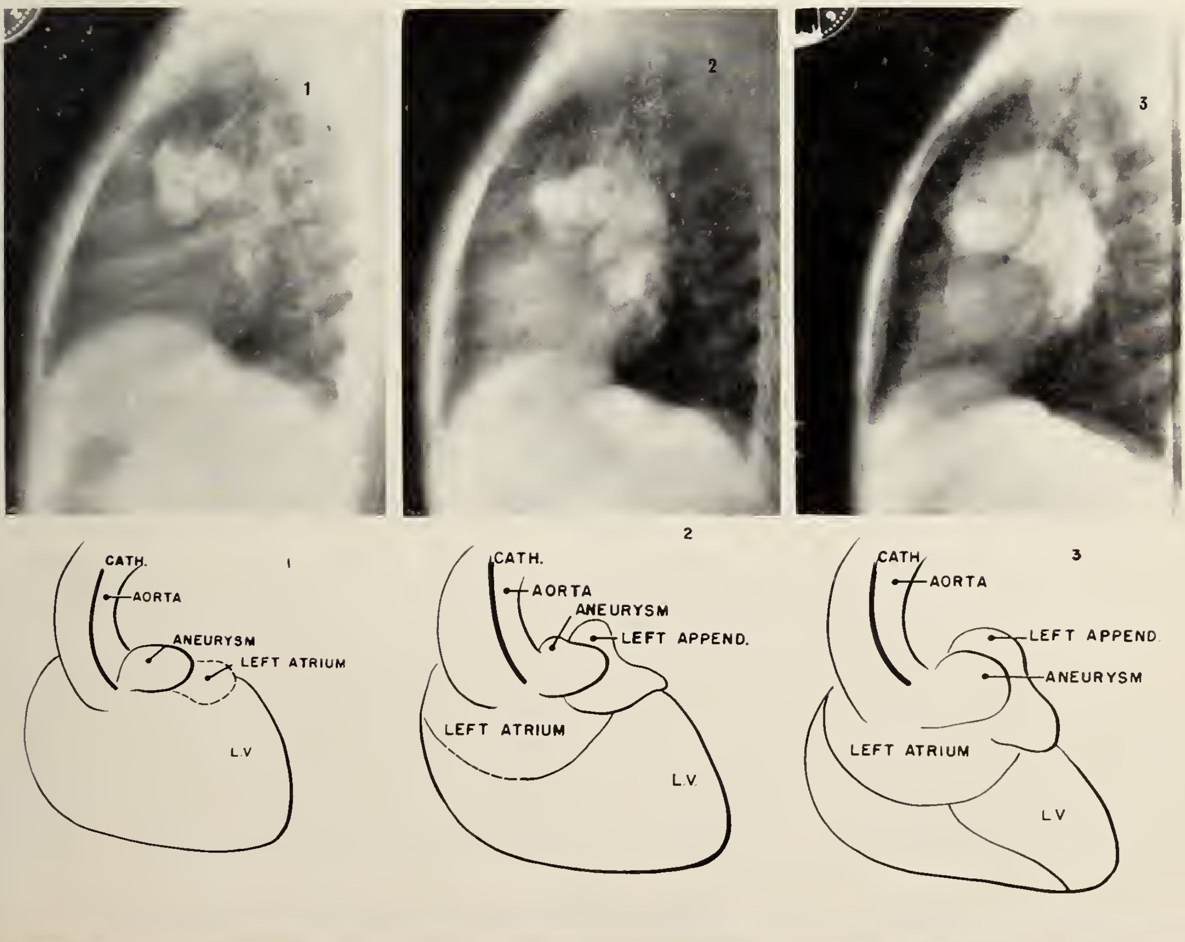


Fig. 6. Aortogram in the posteroanterior and lateral views showing fistula from the aorta to the left atrium. Films were selected from the aortogram series at approximately half second intervals.



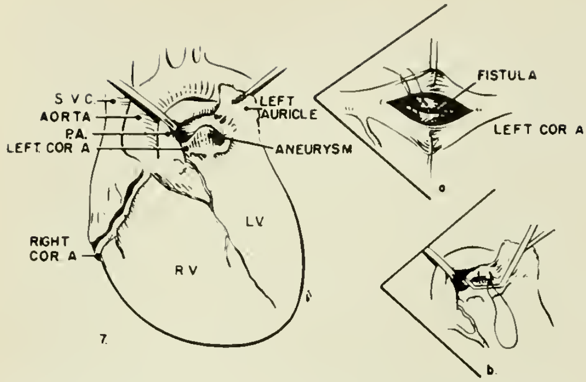


Fig. 7. Drawing showing the fistula and technique of repair

Swan[23] had previously reported a similar procedure in a left coronary to right ventricular fistula using generalized hypothermia of 31.5° C. and caval inflow occlusion for five minutes forty-five seconds in order to avoid injury to a posterior descending branch just proximal to the aneurysm. Although his patient sustained a small diaphragmatic myocardial infarction, he recovered and was well.

SUMMARY

A case report of an almost five-year-old girl with left coronary–left atrial fistula is presented. Preoperative diagnosis was made by angiocardiographic studies. Surgical correction was successfully achieved utilizing extracorporeal circulation.

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Adrenocorticosteroid Hormones and Manganese Metabolism

Effect of Metal Loading

EDWIN R. HUGHES, M.D.
Little Rock, Arkansas

MANGANESE IS essential for normal mammalian growth and reproduction.[1] No definite function has been identified for this element in vivo, and the concentration in mammalian tissues is in micrograms per kilogram.[2] Information regarding the adrenocortical hormones and manganese may be pertinent in two respects: [1] to delineate the homeostasis of the element and [2] to study the mechanism of action of these hormones.

Radioisotope studies of manganese metabolism indicate this metal is rapidly mobile within the body. Using carrier-free radiomanganese (Mn^{54}) and daily whole-body counting, Cotzias and Greenough demonstrated body Mn^{54} turnover was constant at a given dietary intake and rapidly changed when the manganese concentration of the diet was varied or manganese salts were injected parenterally.[3] The isotope is concentrated in organs rich in mitochondria, particularly the liver and pancreas, and the liver may regulate excretion via the bile.[4,5]

Cortisone and cortisol increase the turnover rate of liver Mn^{54} in mice.[6] Injection of the manganous ion (as the citrate) causes a similar increased turnover of liver Mn^{54}.[3] These observations on liver Mn^{54} suggest the hormone and the metal ion are altering manganese metabolism in a similar manner. A major difference exists between the injection of cortisol and the metal, that is, cortisol has no effect on whole-body Mn^{54} turnover, and the metal ion accelerates body turnover proportional to the acceleration of liver turnover.[3]

The experiments reported here were performed to see whether administration of both hormone and metal would result in additive effects on Mn^{54} liver and whole-body turnover. The effect of metal loading on Mn^{54} metabolism in adrenalectomized animals was also tested.

MATERIALS AND METHODS

Male C3H/HeJ, Bar Harbor mice were housed in groups of 5 to 6 and given food and water ad libitum. They were 4 weeks old and weighed 15 to 18 gm. at the beginning of the experiments.

The animals received Purina Chow (manganese = 50 parts per million) with tap water (standard diet), a special diet (manganese = 2 parts per million) with distilled water (low-manganese diet), or a high-manganese diet provided by feeding Purina Chow with drinking fluid containing 1.1 gm. of manganese per liter. The latter diet provided 4 to 6 mg. of manganese per mouse per day.

Carrier-free, $Mn^{54}Cl_2$ received in 20% hydrochloric acid was diluted fiftyfold with sterile saline before intraperitoneal injection of 1.0 μc. Reagent-grade, manganous chloride was dissolved in sterile saline and injected intraperitoneally at a different site to provide an acute load of manganese. The mice were placed 6 cm. above a 3-in. sodium iodide scintillation crystal to assay body radioactivity using a plastic holder to maintain constant geometry. The organs and carcass were placed directly into a 3-in. crystal with a 1-in. well for counting. Radioactivity was recorded in percent of that present at the time of sacrifice or as the percent of the initial dose which was calculated from the whole-body count taken six hours after injection of the isotope.

The fraction labeled GI equaled gut, spleen, and pancreas, while that labeled carcass included all other organs except the liver. The radioactivity in GI is primarily in the gut (90%)

EDWIN R. HUGHES *is with the Departments of Pediatrics and Pathology, University of Arkansas Medical Center, Little Rock.*

TABLE 1

EFFECT OF MANGANESE INTAKE AND ADRENALECTOMY ON BODY DISTRIBUTION OF Mn^{54}*

		Standard diet		High Mn^{54} diet	
Minutes after Mn^{54}	*Part*	*Intact*	*Adrenalectomy*	*Intact*	*Adrenalectomy*
Sixty	GI	46(40-53)	52(48-56)	58(52-62)	36(25-50)
	Carcass	23(20-28)	21(18-24)	21(16-24)	42(20-60)
	Liver	31(25-31)	27(21-31)	21(19-24)	24(15-30)
One hundred	GI	30(22-45)	33(22-51)	38(25-48)	31(24-37)
	Carcass	52(34-60)	50(25-66)	38(25-60)	53(47-56)
	Liver	18(16-21)	17(13-24)	24(14-27)	16(12-22)
Two hundred forty	GI	45(41-49)	44(39-49)	53(50-57)	49(44-53)
	Carcass	30(24-41)	33(29-38)	26(22-29)	30(29-33)
	Liver	25(18-27)	22(21-24)	20(19-22)	21(19-22)

*Recorded as mean and range of percent in the indicated body fractions

and in the carcass, over 90% is in muscle, skin, and skeleton.

The hormone was injected subcutaneously in a dose of 1 mg. per day (50 mg. per kilogram) of either cortisone acetate or 5 mg. every five days of cortisol acetate.

The livers were fractionated in 0.25 molar sucrose, using the equilibrium method described by Westphal.[7] A Spinco model L centrifuge (No. 40 rotor) was employed with the following centrifugal forces: nuclei, 700 g for ten minutes; mitochondria, 5,000 g for ten minutes; and microsomes, 105,000 g for sixty minutes.

RESULTS

Adrenalectomy. Three intact and three adrenalectomized groups were given the high-manganese diet for fourteen days and comparable groups the standard diet. The distribution of Mn^{54} was determined sixty, one hundred, and two hundred forty minutes after intraperitoneal injection; these data are shown in Table 1. Observations after two hundred forty minutes were not made because excretion of the isotope from the animal becomes significant after six hours. Inspection of the data in the first two columns demonstrates that the mean percent of Mn^{54} present in the GI fraction, carcass, and liver at the three time intervals does not differ in adrenalectomized animals compared with their intact controls. At sixty minutes, approximately 50% of the isotope was present in the GI tract with the remainder distributed equally between the liver and carcass. Forty minutes later, GI and liver radioactivity was less (one hundred minute group) with a return at two hundred forty minutes to the distribution observed at sixty minutes.

The distribution of the Mn^{54} in the animals which had been loaded with manganese for two weeks was much more variable, as can be seen by the spread of the data in the last two columns. No striking difference appears in the loaded intact animals (column 3) when compared to the intact animals on the standard diet in the first column, which were on a moderate manganese intake. The loaded adrenalectomized animals (column 4) had a mean GI radioactivity at sixty minutes of 36% compared to 58% for the intact, loaded group, while the carcass radioactivity was higher in these adrenalectomized loaded animals at sixty and one hundred minutes. These data indicate a slower accumulation of the Mn^{54} in the GI fraction of adrenalectomized, manganese-loaded animals.

The livers from the first two sixty-minute groups eating a standard diet were fractionated to ascertain the intracellular distribution of the radioactivity (Table 2). Adrenalectomy had no effect on the intracellular distribution of Mn^{54}, the means for the various fractions being identical.

Adrenocorticosteroid administration. Daily metal injections. Seven groups of mice were placed on the low-manganese diet for three weeks; one group served as control animals while three groups received 0.25 mg. of cortisone acetate and three groups 2.5 mg. of the hormone subcutaneously each day. In addition, one group from each of the different dose levels of hormone

TABLE 2

INTRACELLULAR DISTRIBUTION OF RADIOACTIVE MANGANESE*

	Mn^{54} (percent of total)	
Fraction	*Intact*	*Adrenalectomized*
Nuclear	15(13-17)	15(14-16)
Mitochondrial	50(48-51)	50(48-52)
Microsomal	25(24-26)	25(24-26)
Supernatant	10(9-11)	10(8-11)

*Recorded as mean and range of percent in the indicated fractions

TABLE 3

CARCASS TO LIVER Mn^{54} RATIO, CORTISONE-TREATED ANIMALS RECEIVING DAILY INJECTIONS OF MANGANESE*

Manganese μg. per day	*0*	*1*	*5*
Cortisone mg. per day		*Carcass to liver ratio*	
0	1.3 (1 -1.5)	3.9 (3.4-4.3)	5.4 (5.2- 5.6)
0.25	2.6 (1.5-3.4)	5.2 (3.4-8.1)	10.8 (8.1-14.1)
2.50	3.4 (1.5-7)	6.6 (4.5-8.5)	10.9 (6.1-14.9)

*Data recorded as mean and range of carcass-liver ratios

received intraperitoneally either 0, 1, or 5 μg. of manganese daily. At the end of this period, Mn54 was given intraperitoneally and the carcass to liver distribution of the isotope determined at sacrifice six days later. The data from this experiment are shown in Table 3.

Cortisone accelerated the excretion of radioactivity from the liver increasing the carcass to liver (C/L) ratio in the treated animals. Also, the excretion rate from the liver of the metal injected controls (no cortisone) is faster than from the carcass causing an increase in carcass to liver ratio from 1.3 to 5.4 with increasing metal load. While cortisone increases carcass to liver ratio twofold at the three levels of metal injection, it does not cause discharge of the radioactivity from the whole animal. The lower dose of hormone (0.25 mg. per day) causes the same magnitude of internal redistribution as does 10 times as much cortisone.

Effect of a single large metal injection. Ten groups of animals who had been on the low-manganese diet for three weeks were challenged with loads of metal (5 to 40 μg.) as a single injection at the time they received their radiomanganese. This experiment was performed in groups receiving no adrenal steroid and groups receiving 1 mg. per day of cortisol acetate. Animals were sacrificed, and distribution of radioactivity in carcass, liver, and GI fractions was determined five days after manganese (and Mn54) injection. These data are presented in Table 4. Cortisol administration significantly increased carcass to liver ratio in all groups except the group which received no metal load. The 5-μg. group showed the greatest difference between control, (carcass to liver ratio = 1.9) and cortisol-treated animals (carcass to liver ratio = 6). Carcass to liver ratios and body distribution data at sacrifice do not take into account the accelerated excretion of the Mn54 after metal load. These data are presented graphically in Figure 1 as percent of the initial dose found in the liver at five days. The injection of 5 μg. of manganese per mouse (250 μg. per kilogram) decreases liver radioactivity to 8.7% at five days in the control and 2.4% in the hormone-treated mice. A proportionally smaller amount of the tag is altered by the hormone as the metal load is increased beyond 5 μg. There is no difference in the rate of body turnover of the isotope between control and cortisol-treated groups. Typical, whole-body turnover curves for two control and two treated groups at the lowest and highest levels of metal load are shown in Figure 2.

DISCUSSION

The results of these experiments confirm the previously reported adrenal glucocorticoid effect on

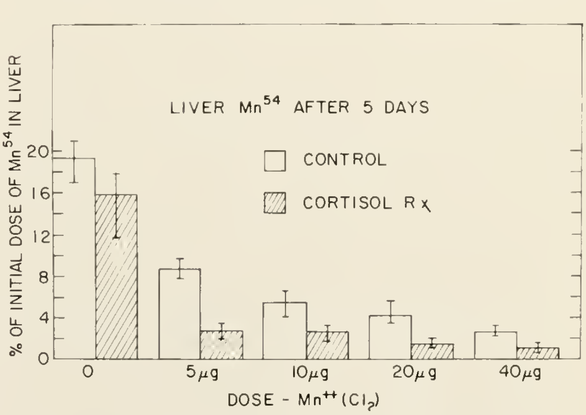

Fig. 1. The radioactivity present in the liver is shown as percentage of the initial dose rather than percent in the whole animal as in Table 4. The bars enclose the range of all data for six animals.

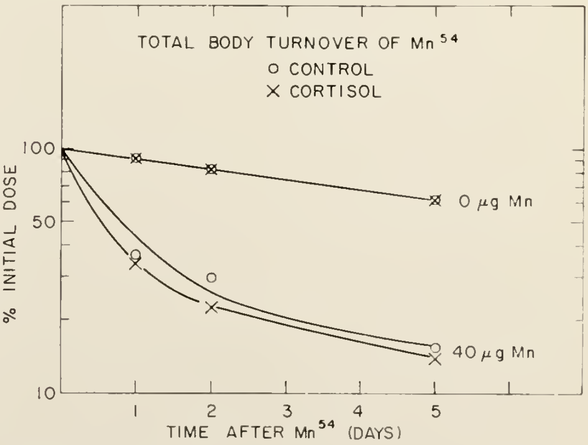

Fig. 2. The whole body turnover of Mn^{54} is shown for the group receiving the smallest and largest amounts of injected manganese in control mice and those receiving cortisol acetate in a dose of 1 mg. per day. This illustrates the absence of glucocorticoid effect on whole-body turnover of radiomanganese. Each point is the mean for six animals.

TABLE 4

EFFECT OF A SINGLE LARGE INTRAPERITONEAL MANGANESE INJECTION ON BODY DISTRIBUTION OF Mn^{54}*

µg. of manganese injected	*Control*				*Cortisol*			
		Percent in				*Percent in*		
	Carcass	*Liver*	*GI*	*C/L*	*Carcass*	*Liver*	*GI*	*C/L*
0	40	32	28	1.3 ± 0.1	48	26	26	1.8 ± 0.5
5	50	26	24	1.9 ± 0.1	70	12	18	6.0 ± 0.4
10	53	20	27	2.7 ± 0.7	67	12	21	5.4 ± 0.6
20	55	21	24	2.4 ± 0.2	78	9	13	8.7 ± 1.0
40	58	18	24	3.4 ± 0.7	75	9	16	8.2 ± 1.7

*Recorded as mean percent of radioactivity in the indicated fractions. Carcass to liver (C/L) ratios are recorded as mean and standard deviation.

radiomanganese metabolism[6] at two levels of dietary intake of manganese and with simultaneous parenteral loading. This effect, the elution of Mn^{54} from the liver without change in the whole-body turnover, is related to the amount of body manganese. When the animal is relatively depleted, glucocorticoid administration has less effect on Mn^{54} distribution (Table 4). However, in manganese replete animals, adrenal corticosteroid readily produces the redistribution. Metal injection appears to make the liver isotope more exchangeable and available for elution by the adrenal glucocorticoid.

In the experiment where the dose of glucocorticoid was held constant at 1 mg. per day and 0 to 40 µg. of manganous ion injected as a single injection, a limit to the proportion of liver Mn^{54} which could be eluted was approached at the 5-µg. manganese level (Fig. 1); greater amounts of metal produced only minimal further decrease of liver radioactivity or increase of the carcass to liver ratio. This effect was, however, only an internal body redistribution of Mn^{54}. There was, in addition, an acceleration of the whole-body turnover when the metal ion was injected, which was not influenced by hydrocortisone administration (Fig. 2).

The significance of the 5-µg. load of metal in terms of manganese requirements by the mouse is not known. The low-manganese diet used contains approximately 2 µg. of manganese per gram. At this dietary level, however, the liver manganese available for elution by glucocorticoids was diminished.

Since the metal load was important for producing a change in the rate of Mn^{54} distribution by glucocorticoids, it was expected that adrenalectomy would alter the rates of distribution of Mn^{54} in the metal-loaded mouse. That this is true is suggested by the sluggish rate of appearance of Mn^{54} in the GI fraction of the body pool in the adrenalectomized animals on a high-manganese diet (Table 1). These data cannot be interpreted definitively, for it is not known whether the radioactivity is in the lumen of the gut or in the cells of the gut wall and mesentery.

If the lower radioactivity in the GI fraction at sixty minutes represents a lesser proportion of intraluminal isotope, this can be interpreted as a less rapid excretion of isotope by the liver in the adrenalectomized, metal-loaded animal. The fall in liver radioactivity between sixty and one hundred minutes in both intact and adrenalectomized animals on a standard diet agrees with the hypothesis that one major route of manganese excretion is via the liver and bile.[5] Intact animals on the high-manganese diet did not show a drop in the liver radioactivity over the six hours, which may reflect a continual secretion of administered radioactivity during the observation period. However, in contrast to the adrenalectomized animals, the intact animal was able to excrete the tag into the GI tract rapidly, which is reflected in the high percentage of radioactivity at sixty minutes.

It has been suggested that one major route of manganese excretion is via the liver and bile. Thus, if the lower proportion of radioactivity in the GI fraction of the adrenalectomized, manganese-loaded animals (Table 1, column 5) represents a lesser quantity of intraluminal isotope, the greater proportion in carcass at sixty and one hundred minutes might be interpreted to indicate a lesser rate of hepatic biliary excretion of Mn^{54}. The lesser proportion of liver Mn^{54} at one hundred minutes in adrenalectomized animals would also agree with such a hypothesis.

SUMMARY

The effect on radiomanganese kinetics of varying the level of adrenocortical function and manganese load was tested in mice. The magnitude of elution of tracer Mn^{54} from the liver by glucocorticoids is dependent on the amount of metal available to the animal. At least 5 µg. of metal is necessary for near maximal elution of tracer from the liver by cortisol in a partially deficient mouse.

Adrenalectomy has an effect on Mn^{54} kinetics only when the animals are subjected to large dietary loads of manganese.

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ADMINISTRATION OF 5-FLUOROURACIL (5FU) is the primary treatment for disseminated breast cancer in women who are between menopause and ten years postmenopause. Although oophorectomy should be tried first in premenopausal women and hormone therapy in women who are more than ten years past menopause, 5FU therapy should be initiated if the disease is still progressing six weeks after oophorectomy or hormone treatment. The agent is given cautiously to its maximum potential, preferably until some drug reaction indicates adequate dosage. The current standard dosage is 12 mg. of 5FU per kilogram of body weight per day for four or five days, then half doses on alternate days. The patient is examined thirty days after the end of the course, and if progression is apparent, other therapy is substituted. If no progression is observed, courses are repeated at thirty-day intervals until progression occurs. Occasionally, osseous metastases increase slightly after the first course, in which case another is given. One to 12 courses of 5FU therapy administered to 255 patients resulted in only 1 toxic death.

F. J. ANSFIELD, M.D., University of Wisconsin, Madison. The indications for 5-fluorouracil in the treatment of breast cancer. Geriatrics 20:250-253, 1965.

Rupture of the Stomach

Clinical and Experimental Study

M. JOYCELYN ELDERS, M.D., and EDWIN R. HUGHES, M.D.
Little Rock, Arkansas

RUPTURE OF THE STOMACH in a newborn infant is a rare but catastrophic event. Sporadic reports have appeared in the literature since 1825, and multiple etiologic factors have been suggested for this entity.[1] A case of spontaneous rupture of the stomach occurred in this hospital in a premature infant who had been fasted seventy-two hours and subsequently received an intravenous infusion of epinephrine. Eighteen hours later the infant was in shock and expired.

The hemorrhagic necrosis of the stomach wall in this case and those reported[2,3] was reminiscent of lesions experimentally produced in the rabbit mesoappendix by gram-negative endotoxin and aggravated by epinephrine.[4] In considering the pathogenesis of this lesion, the adrenal glucocorticoids came to mind since these hormones are reported to be ulcerogenic[5] and since they inhibit connective tissue growth.[6]

Increase in intragastric pressure has been suggested as the cause of spontaneous gastric rupture. This explanation would be satisfactory if the stomach wall ruptured at low pressure or if structural defects could be identified. Neither of these possibilities has been confirmed. No information on pressure necessary for rupture of the human stomach is known to the authors.

This paper reports a case of spontaneous rupture of the stomach and the results of experiments designed to determine the pressure which causes rupture of the obstructed human infant stomach and the predominant site of artificial rupture. Studies in mice are reported where gastric rupturing pressure was determined after fasting and Salmonella typhosa endotoxin, epinephrine, salicylate, or prednisone administration.

CASE REPORT

The patient was born prematurely (weight 2.1 kg.) to an 18-year-old woman whose VDRL was negative. The prenatal course and delivery were not complicated and no abnormal physical signs were present at birth or during the first four days of life. The infant was included in a metabolic study as a normal premature infant. After a seventy-two-hour fast, the blood glucose was 35 mg. percent and increased to 66 mg. percent one hour after administration of 0.06 μg. epinephrine intravenously. Following this study (thirty-six hours before death) the patient was started on oral feedings of 5% dextrose in water, followed by formula feedings every three hours. Eighteen hours after beginning oral fluids, the infant was noted to be distended, dyspneic, cyanotic, and jaundiced. Laboratory data at this time included: hemoglobin 16.2 gm. percent, white blood count 2,700 cu. mm., differential count 18% polymorphonuclears, 79% lymphocytes, and 3 metamyelocytes. Blood urea nitrogen was 30 mg. percent, CO_2 binding capacity 12 mEq. per liter, sodium 124 mEq. per liter, chlorides 96 mEq. per liter, and bilirubin 7.9 mg. percent. There was no growth of bacteria in blood and cerebrospinal fluid cultures. A roentgenogram of the abdomen taken three hours before death was interpreted as showing free gas in the peritoneal cavity and pneumatosis cystoides intestinalis (Fig. 1).

A clinical diagnosis of bacterial septicemia was made eighteen hours before death and the infant received intravenous fluids and antibiotics. The definitive diagnosis of rupture of an abdominal viscus was made two hours before death and the infant expired before surgery.

At autopsy gross findings included: jaundice, cyanosis, edematous induration of the abdominal wall, atelectasis of both lungs, air and gastric contents in the peritoneal cavity, generalized peritonitis, and subserosal pneumatosis cystoides intestinalis throughout the small and large bowel. The stomach had ruptured on the greater curvature high in the fundus (Fig. 2). The gastric wall was severely congested with blood, but no other defects were found in the mucosa or wall. Microscopic sections confirmed the presence of atelectasis in the lungs. Polymorphonuclears were seen on the serosa of all abdominal viscera and subserosal air spaces were present in all intestinal sections. Sections taken at 6 different sites be-

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M. JOYCELYN ELDERS *and* EDWIN R. HUGHES *are from the departments of pediatrics and pathology, University of Arkansas Medical Center, Little Rock.*

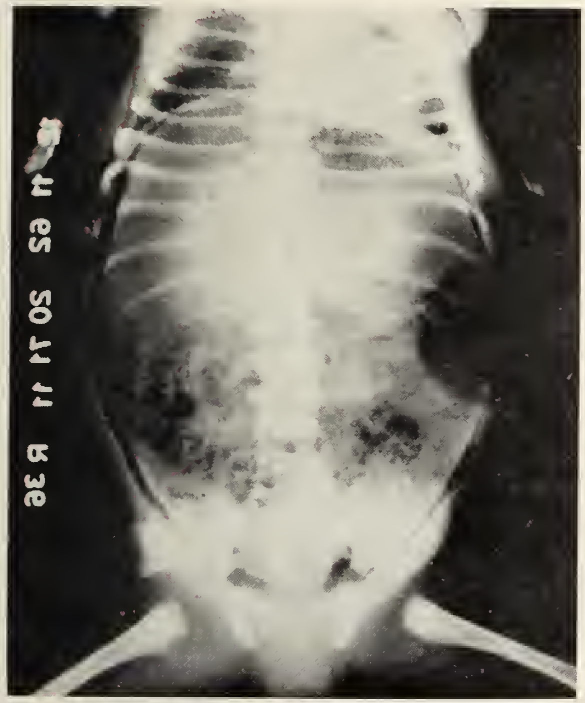

Fig. 1. Roentgenogram of the abdomen three hours before death

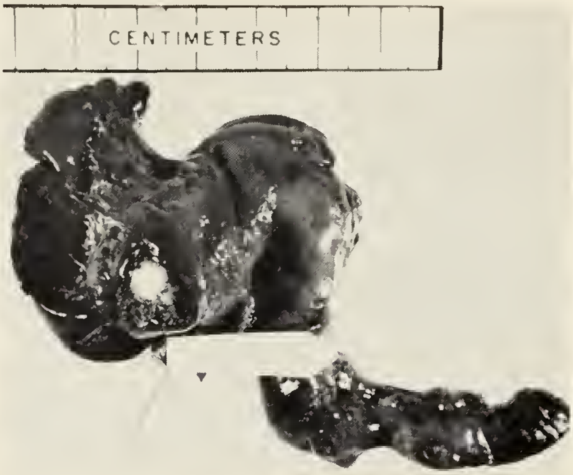

Fig. 2. Photograph of the autopsy specimen which includes the stomach, spleen, and upper duodenum. A probe has been inserted into the esophagus and a cotton ball into the lumen of the stomach. The site of rupture can be seen high in the fundus on the greater curvature with the white cotton ball defining the size of the rupture

tween the cardia and pylorus all showed severe congestion of submucosal vessels (Fig. 3). Separation of muscle bundles, necrosis, and acute inflammatory cells were seen at the site of rupture. No vascular thromboses were found in the stomach wall or major abdominal vessels.

EXPERIMENTAL METHOD

Stomachs were obtained from 17 consecutive pediatric patients over a two-month period within two to twenty-four hours following death. The mice used were weanling CH3/HeJ Bar Harbor strain and were housed in groups of five. The intragastric pressure at the time of rupture was measured using a Beckman-Offner RB Dynograph connected to a 5-mm. glass cannula (human stomachs) or a No. 15 needle with a 3-mm. grooved flange (mouse stomachs). The cannula was secured in place in the esophagus (human stomachs) or in the duodenum (mouse stomachs) using heavy suture material. The opposite end of the stomach was tied and air delivered at the rate of approximately 60 cc. per minute (infant) and 20 cc. per minute (mouse) through a needle valve while the pressure was continuously recorded. This rate of inflation caused the stomach of both the human and the mouse to rupture at 100 ± 20 seconds. Tissue was fixed from the site of rupture for histologic examination in selected instances.

Twelve groups of mice (5 to 10 per group) varying in age from 4 to 12 weeks were studied in 6 separate experiments. Except for the seventy-two-hour fast experiment, all other groups were fasted sixteen hours before study. The control group for the seventy-two-hour fasted group was fed until the time of sacrifice. Each

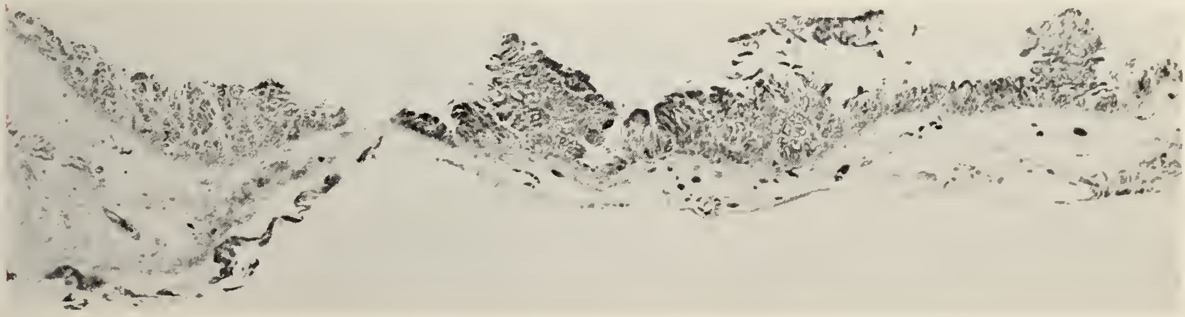

Fig. 3. Low power (× 50) view of a section taken from the stomach of the case being reported close to the site of rupture

TABLE 1

GASTRIC RUPTURING PRESSURE IN INFANTS

Case number	*Age (days)*	*Weight (kg.)*	*Cause of death*	*Rupture site*	*Pressure (mm. Hg)*
1	14	3.3	Congenital heart disease	LC*	81
2	2	1.9	Intracranial hemorrhage	LC	105
3	5	1.9	Duodenal atresia	LC	115
4	14	2.6	Diarrhea	LC	120
5	1	3.0	Intracranial hemorrhage	GC†	55
6	7	3.6	Anencephaly	LC	185
7	14	4.7	Perforation of ileum	LC	80
8	1	1.3	Hyaline membrane disease	GC	100
9	135	3.0	Infantile spasms	GC	65
10	1	4.6	Traumatic delivery	LC	80
11	49	3.0	Congenital heart disease	GC	115
12	42	1.0	Prematurity	LC	125
13	40	1.4	Pneumonia	LC	122
14	11	3.1	Meningitis	LC	120
15	2	1.8	Thrombocytopenia	GC	95
16	8	3.5	Anencephaly	GC	320
17	42	2.8	Brain damage	LC	110
Mean	23	2.7		GC/LC =6/11	117
Range	(1-135)	(1-4.7)			(55-320)

*Lesser curvature
†Greater curvature

TABLE 2

GASTRIC RUPTURING PRESSURE IN MICE

Experiment		*N*	*Pressure* (mm./Hg)*
I.	Control (fed)	10	86 (68-105)
	Seventy-two-hour fast	10	81 (70-100)
II.	Control	10	80 (72-88)
	Epinephrine	10	84 (70-96)
III.	Control	7	68 (64-70)
	Endotoxin	7	68 (60-78)
IV.	Control	5	94 (85-100)
	Epinephrine plus endotoxin	5	105 (93-116)
V.	Control	6	77 (70-88)
	Salicylate	6	76 (60-88)
VI.	Control	7	77 (68-88)
	Prednisone	7	53 (40-65)

*Mean with range of all values

experiment was conducted by rupturing stomachs from a control and experimental group, in an alternate fashion. This decreased the likelihood of differences being due purely to technical difficulties with the apparatus. The experimental groups were as follows:

I. Fasted seventy-two hours
II. Epinephrine, 100 μg., intraperitoneally twenty minutes before study
III. Salmonella typhosa endotoxin (Difco A lipopolysaccharide No. 901) 0.5 mg., intraperitoneally twenty hours before sacrifice
IV. Same as group III but also given epinephrine, 100 μg. intraperitoneally twenty minutes before study
V. Sodium salicylate, 240 mg. per kilogram daily by mouth for fourteen days
VI. Prednisone 10 mg. per kilogram daily by mouth for fourteen days

RESULTS

Human material. The pressure necessary to rupture the stomach of 17 consecutive infants dying in this hospital with a mean age of 23 days and mean weight of 2.7 kg. is shown in Table 1. The primary cause of death and the experimental rupture sites are also listed. The rupture site occurred twice as frequently on the lesser curvature as compared to the greater curvature. The mean rupturing pressure for this group of infants was 117 mm. Hg (2.26 lb. per square inch) with a range from 55 to 320 mm. This group is too small and heterogenous to attempt correlation between either disease process or therapy and the site of rupture or rupturing pressure. However, it is odd that the two highest pressures found occurred in anencephalic infants. Seven stomachs were filled with food at the time of rupture; the mean pressure was 134 mm. Hg (SD = 87). Ten stomachs were empty at the time of rupture; the mean pressure was 106 mm. Hg (SD = 20). These means do not differ significantly.

Animal studies. The mean rupturing pressure in the control groups which were fasted sixteen hours ranged from 68 to 94 in the 5 separate experiments on 5 different days (Table 2). This variation in control pressures may have been due to differences in the rates of flow of air used to rupture the stomach. Since control and experimental stomachs were ruptured in an alternate fashion, this variation does not invalidate comparison of the 2 groups on a particular day.

As can be seen, the seventy-two-hour fast, epinephrine, endotoxin, and salicylate groups are not different from their controls. The mean rupturing pressure found in the endotoxin plus epinephrine group is 11 mm. higher than the control group, but there is almost complete overlap of the data.

The administration of prednisone in a dose of 10 mg. per kilogram per day lowered the mean rupturing pressure 24 mm. and there is no overlap of data when compared to controls. This dose

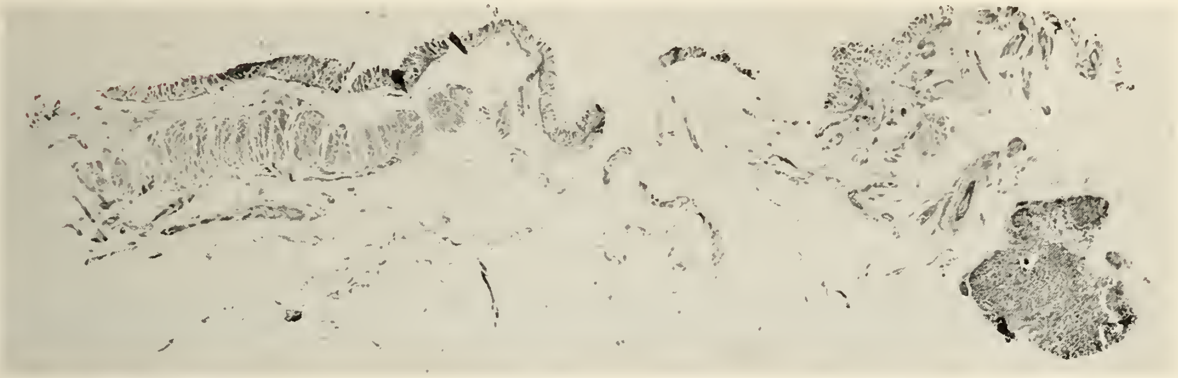

Fig. 4A. Low power (× 50) view of a section taken from an infant's stomach which was artificially ruptured

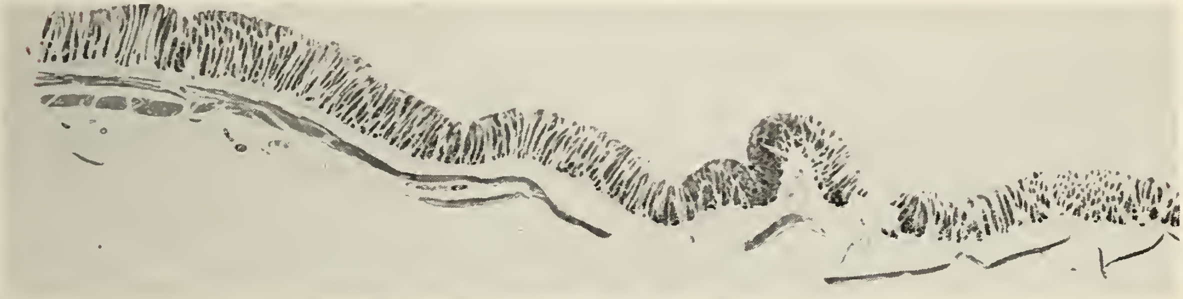

Fig. 4B. Similar view taken from a control mouse stomach which was artificially ruptured

produced growth inhibition in the animals but they were otherwise in good condition.

GROSS AND MICROSCOPIC FINDINGS

None of the experimental maneuvers used here produced submucosal hemorrhage which was similar to that seen in the reported human case. Microsections taken from the area of rupture did show separation of the muscle bundles in both the human and mouse material (Figs. 4A and 4B). Grossly and microscopically, the gastric walls from mice and premature infants had much smaller muscle bundles and an apparent lesser muscle mass than did the stomachs from term infants and older children. Excluding the control group which was fed, 75 of the 80 mouse stomachs studied after fasting ruptured on the lesser curvature near the cardia. In the fed control group, where the stomach was filled, the site of rupture was on the greater curvature in 7 of the 10 animals. Of the human stomachs studied, 7 of the 10 which were empty ruptured on the lesser curvature while 4 of the 7 stomachs with food ruptured on the greater curvature.

DISCUSSION

Only 15 cases of gastric perforation were recorded in the literature by 1943.[2] This entity would appear to be more common than the older literature indicates since Inouye and Evans were able to find 143 reported cases and added 6 new cases in 1964.[1] McCormick surveyed autopsy cases under two months of age and found an incidence of 1:444.[7]

Multiple etiologies have been suggested by various authors.[1] Two major categories emerge in the reported cases: acute gastric ulcer and congenital absence of gastric musculature. These categories account for one-half of the reported cases, the cause of the remainder being undetermined or related to trauma, sepsis, gastrointestinal obstruction, etc. If the perforation is not due to an acute gastric ulcer, the pathogenesis of the rupture is not clear in the majority of cases. Kneiszl[8] carefully studied 15 stomachs from premature and newborn infants and concluded it is not reasonable to consider absence of musculature a pathologic state or developmental anomaly since gaps are normally present. He proposes that the greater curvature high in the fundus is the weakest site, since, at this site, gaps were more frequent and larger and this would determine the site of rupture regardless of etiology.

The site of rupture in these experiments using air was consistently on the lesser curvature when the animals were fasted and not at the site proposed as having the least musculature. Since the lesser curvature has the shortest longitudinal distance, rupture on this border would be expected during artificial distention and it would appear that this mechanism is not operative in the reported human cases. However, when the animals had stomachs which were distended with food, the site of rupture was high in the fundus on the greater curvature even though the air was being introduced through the pylorus. It would appear the presence or absence of a full stomach can affect the site of rupture.

From the data presented, it seems apparent that the thickness of the wall is not the major factor in determining its strength since the pressure necessary to rupture a mouse stomach is similar to the pressure needed for a six-week-old child. Also, there was no correlation between the weight or age of the infant and the gastric rupturing pressure. In the human infant presented, fasting and epinephrine administration were temporally so closely related to the gastric rupture it seemed reasonable to ask "Do these factors alter the strength of the gastric wall?"

This seemed unlikely since epinephrine lowers splanchnic resistance and would increase blood flow to the stomach.[9] However, on reviewing the reports of Zweifach and associates[4] and Jacobson and co-workers,[10] the combined effect from epinephrine and endotoxin might reduce blood flow resulting in ischemic necrosis. The data collected in mice (Table 2) do not support this postulate, since large doses of epinephrine and endotoxin did not alter gastric rupturing pressure. The administration of high doses of adrenocortical hormones reduced the rupturing pressure. The explanation for this effect is presumed to be inhibition of connective tissue growth.[11] Salicylates also inhibit connective tissue growth [12,13] but did not alter rupturing pressure in the dose used in these experiments. No ulcerations were present in stomachs from either group.

The pressure necessary to rupture a human stomach had not previously been systematically studied. Farber and Vawter[14] mentioned in a discussion that a pressure of the order of 200 to 280 mm. Hg was necessary. This is considerably higher than the mean pressure found in the present study. It seems unlikely that gastric pressures of the order of 100 to 200 mm. Hg could be produced in vivo by an oxygen mask. It is theoretically possible that rupture might occur with lesser pressure if the stomach wall has been previously compromised by interruption of blood flow, endotoxin, increased adrenal corticosteroid levels, or other factors. Results of the present studies do not explain pathogenesis of the lesion found in spontaneous rupture of the stomach in the newborn. "Stress" (adrenocortical stimulation) may be a contributing factor.

SUMMARY

A case of gastric rupture is reported in a premature infant. In addition, experimental studies are also reported on the rupturing pressure of the stomach in humans and mice.

The mean rupturing pressure of stomachs from infants 0 to 135 days of age was 117 mm. Hg. The mean pressure for groups of mice was 68 to 94 mm. Hg. Fasting, epinephrine, endotoxin, and salicylates did not alter the gastric rupturing pressure in mice. High doses of prednisone did lower the pressure, but did not produce the submucosal hemorrhage characteristic of the natural disease in the human.

The site of rupture was more frequent on the lesser curvature when the stomach was empty and on the greater curvature when it was full.

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The authors thank Mrs. Bernice Parham and Miss Ann Smith for technical assistance and Mrs. Ann Haydon for preparation of the manuscript.

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Subacute Sclerosing Leukoencephalitis in Association with Toxoplasmic Encephalitis

JOHN H. BORNHOFEN, M.D., and
MARY ELIZABETH RICHARDSON, M.D.

Little Rock, Arkansas

Many authors[1–3] are now of the opinion that van Bogaert's subacute sclerosing leukoencephalitis, Dawson's subacute inclusion body encephalitis, and the nodular panencephalitis of Pette-Döring represent a single nosological entity. Although slight differences exist in the site of the histological lesion, the clinical course and the laboratory data are strikingly similar. The etiology of any of these three conditions, however, whether considered separately or as a single entity, remains in doubt. Because of the character of the inflammation and the presence in many cases of type A intranuclear inclusions, it is believed that a virus is the causative agent.[4] In spite of many attempts, however, in only a few cases has an organism been identified. Foley and Williams[5] isolated an agent which, after repeated passages through young mice, behaved very similarly to known herpes simplex. Martin and associates[6] succeeded in isolating a virus encephalogenic for the mouse, but its exact nature was not identified. Gullotta and Wechsler[7] noted in one case complement-fixation reactions for Coxsackie A-2 and B-1. In two separate case reports,[8,9] the onset closely followed smallpox vaccination, and Simpson[10] noted three cases with a preceding history of infectious hepatitis. To Pette and Döring,[11] the pathologic findings in nodular panencephalitis were strongly reminiscent of type B encephalitis. It has also been pointed out[12] that the histological picture of subacute sclerosing leukoencephalitis has similarities to that seen in general paresis and that it resembles both clinically and pathologically the changes in cerebral trypanosomiasis. A recent epidemiological report from Belgium[13] makes note that subacute sclerosing leukoencephalitis occurs more frequently in rural than in urban areas and in low-lying than in hilly country and is more prevalent among manual workers and the lower social classes. Unexpected deaths among animals in the immediate neighborhood have also been noted. In view of these varying etiologies, van Bogaert[14] has questioned whether the characteristic changes of subacute sclerosing leukoencephalitis could not be regarded as constituting a single mode of reaction of the central nervous system to various insulting agents.

In this report, a case clinically identical to subacute sclerosing leukoencephalitis is presented. The child, during the course of the illness, developed typical toxoplasmic chorioretinitis associated with a positive Sabin-Feldman dye test. Postmortem examination of the brain revealed multiple cysts of Toxoplasma organisms within the central nervous system, plus the gliosis and chronic perivascular reaction of a subacute encephalitis.

CASE REPORT

A white male, born Dec. 26, 1956, was the third of four children. The family was of low socioeconomic status; the parents were divorced. There was no family history of neurological disease. The child was the product of a pregnancy complicated by abdominal cramping at the fifth month and subsequent fainting spells, nausea, and vomiting. Delivery occurred at term, forceps being used after thirty-six hours of labor. The birth weight was 6 lb. 2 oz. There was no neonatal distress. The neuromotor development compared favorably to that of the siblings. The child may have had a brief unconscious episode from contact with an electric wire at the age of 5 months. There were no noted sequelae.

A gradual personality change with fearfulness and irritability was noted beginning about age 6 (October 1962). The schoolteacher requested an intelligence test because of the child's failure to achieve. Several weeks later, while in school, the child experienced a light seizure manifested by clonic shaking of the left arm and limpness of the legs. Upon arising from his desk, he stumbled and ran into a wall. Several days later a second seizure of sudden onset occurred, with forceful extension of the trunk and rotation to the left, elevation of the arms, and momentary unconsciousness, followed

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JOHN H. BORNHOFEN *is assistant professor, Departments of Pediatrics and Neurology, and* MARY ELIZABETH RICHARDSON *is assistant professor, Department of Pathology, University of Arkansas Medical Center, Little Rock.*

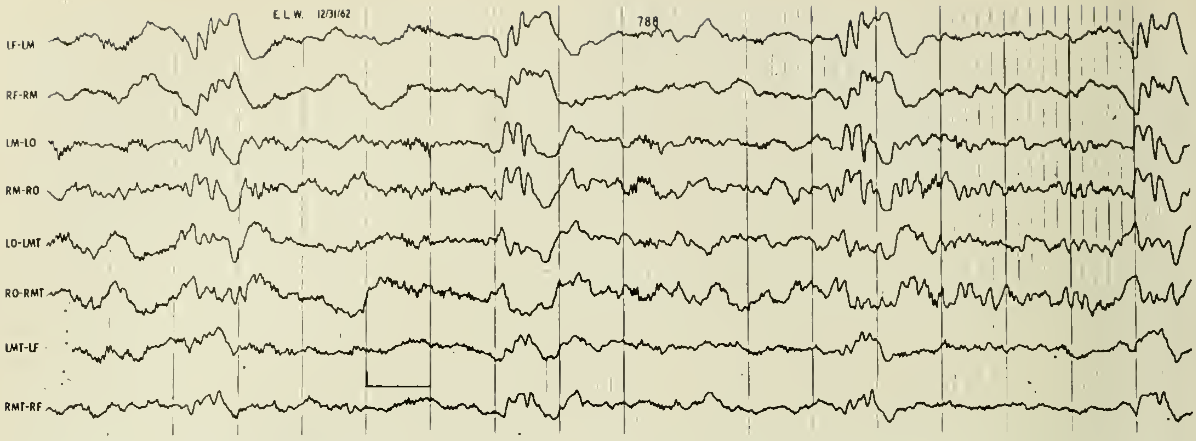

Fig. 1. Initial electroencephalogram two months after onset of illness revealing rhythmic generalized bursts of high-voltage slow waves during sleep

by transient lethargy. He developed a broad-based unsteady gait and was hospitalized. There he was noted to develop recurrent myoclonic movements of the extremities that gradually became rhythmic. Rapid deterioration of motor ability occurred with inability to walk or crawl. By the fourth month of illness (February 1963), his attention could be reached only occasionally. Because of progressive unresponsiveness and inability to take oral fluid, he was transferred to the Fort Worth Children's Hospital.

Neurological examination at that time revealed an obtunded, emaciated boy with poor dental hygiene. Intermittently he manifested rhythmic dystonic movements of the right arm or leg, with slight turning of the head and eyes to the right. He occasionally smiled briefly and seemed able to understand partially, making poorly enunciated "yes" or "no" sounds. He was able to follow with the eyes; however, there was no apparent upward conjugate gaze. The pupils reacted to light, and the optic fundi were normal. There was slight nuchal rigidity. The muscle tone was decreased except in the left arm, where there was slight increased muscle tone with a suggestion of cogwheeling. The deep tendon reflexes were very brisk in the lower extremities. Stretch reflexes were present at the ankles, and the Babinski sign was present bilaterally. There was an active jaw jerk.

Laboratory studies were as follows: Complete blood count, urinalysis, and blood chemistries were within normal limits. The blood serology was negative. Examination of the cerebrospinal fluid on two occasions revealed no cells and protein of 38 to 40 mg. percent; colloidal gold curves were 5555431000, and the report from the VDRL was negative. An electrophoretic pattern of the cerebrospinal fluid was normal. A pneumoencephalogram performed on March 1, 1963, revealed a normal ventricular system. A gallbladder visualization study revealed normal filling, and an electrocardiogram was within normal limits. Numerous electroencephalograms were obtained during the course of the illness (Figs. 1 and 2). These revealed an emerging pattern of recurrent, somewhat stereotyped bursts of slow waves occurring semirhythmically, with gradual slowing of the background activity. In addition, frequent high-voltage spike discharges were seen in either frontal area. In the final electroencephalogram, an essentially flat record appeared.

Course. The child gradually became less responsive. In the seventh month of illness (April 1963), a fluffy, white exudative lesion not noted on previous examinations was seen in the macular area of the right optic fundus. Over the next several weeks this evolved into the pigmented, irregular, scarred lesion suggestive of toxoplasmosis. At that time, the methylene blue dye

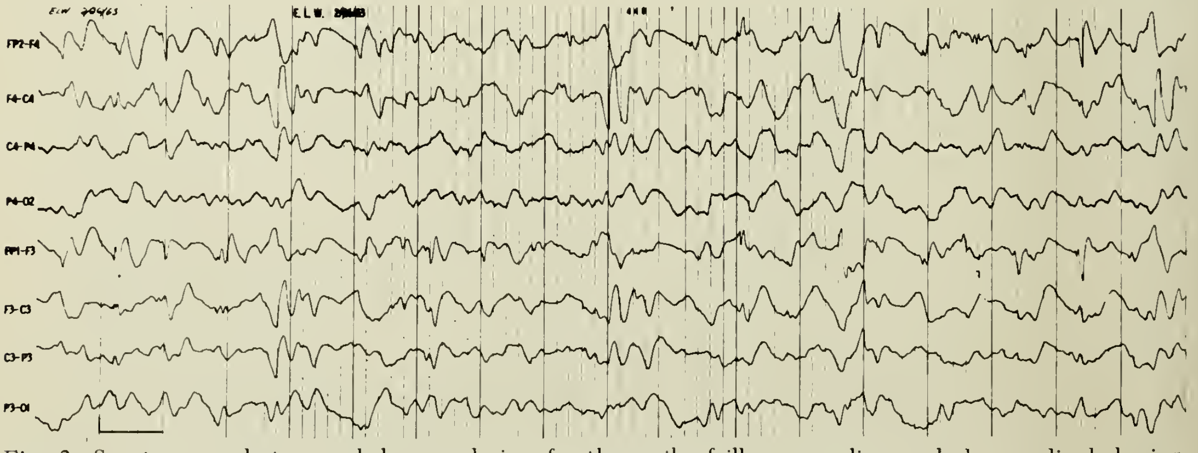

Fig. 2. Spontaneous electroencephalogram during fourth month of illness revealing marked generalized slowing, recurrent bursts of high-voltage slow waves, and focal spikes in either frontopolar area

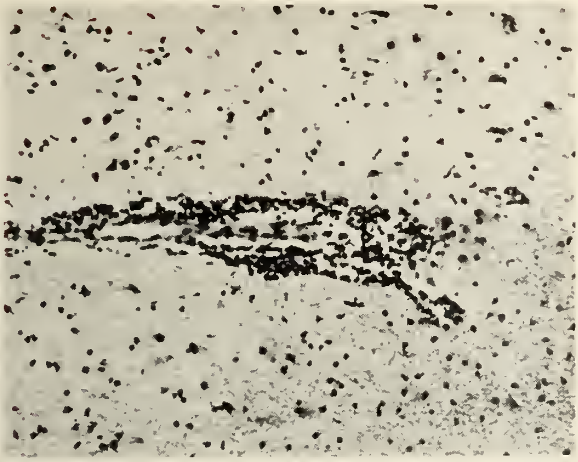

Fig. 3. Original biopsy of cerebral cortex with perivascular infiltrate around small vein. Hematoxylin and eosin, × 200

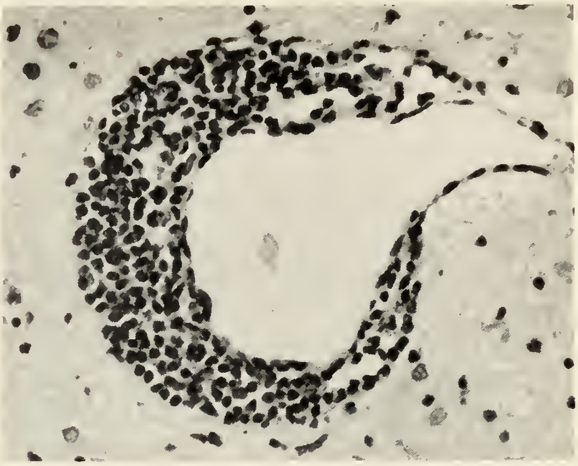

Fig. 4. Vein in centrum ovale showing infiltration of sheath and perivascular space by chronic inflammatory cells. Hematoxylin and eosin, × 400

titer for toxoplasmosis was 1:1,024 and the complement-fixation test was 1:64. Two successive dye titers at monthly intervals were still 1:1,024; normal is equal to or less than 1:256. In March 1963, a frontal lobe brain biopsy was performed. The child expired during a bout of high fever on Nov. 5, 1963, after thirteen months of illness.

Brain biopsy findings. Microscopic examination of the cerebral biopsy material of March 1963 revealed many chronic inflammatory cells, predominantly lymphocytes, in focally thickened meninges, surrounding thin-walled vessels within the meninges and in the underlying brain substance (Fig. 3). There was marked thickening of the walls, with luminal narrowing of many of the small arteries of the meninges and of the brain. Neuronal loss was present in all layers of the cortex, with striking nuclear pyknosis and loss of Nissl substance from the majority of the residual neurons. Increased glial elements were present. The underlying white matter showed focal demyelinization.

Autopsy findings. Gross findings at autopsy outside of the central nervous system were essentially noncontributory. Cerebral edema and atrophy were noted. Microscopic sections of the brain demonstrated more advanced atrophy than the original biopsy. Chronic inflammatory cells were still prominent in the meninges and around thin-walled vessels (Fig. 4). Small arteries in the meninges and gray and white matter were remarkably thickened and frequently hyalinized (Fig. 5). Scattered glial nodules were present (Fig. 6). The cortex was characterized by a striking reduction in neurons and an increase in glial elements. Definite inclusion bodies could not be identified in any of the shrunken residual ganglion cells. The centrum ovale from all parts of the cerebral cortex showed extensive spongy degeneration, with cystic areas containing scattered lipid-laden compound granular corpuscles. The surrounding tissue frequently contained many reactive astrocytes. Also present in this glial tissue were many cells containing numerous spherules, 3 to 10 μ in diameter, consistent with toxoplasma organisms. Although these were found with difficulty in the routine hematoxylin and eosin stains, the organisms were readily demonstrable with phloxine B as clumps of spherules, each with a central red area surrounded by a thin rim of pale blue cytoplasm (Fig. 7). A cell nucleus was readily identified in many of these pseudocysts. In other clusters, a cell nucleus could not be found and the cell membrane was not distinct. A few groups of organisms were found beneath the ependyma and in the cortex. An ependymitis was not present. A single small focus of calcium was noted.

DISCUSSION

As has been pointed out by many authors, the clinical and laboratory findings associated with subacute sclerosing leukoencephalitis, subacute inclusion body encephalitis, and nodular panencephalitis are quite similar. The conditions affect primarily children and young adults, with a predominance of males to females. The onset is usually one of insidious personality change. Behavioral disturbances, inattentiveness, and paucity of speech are seen, associated with declining school performance and evidence of intellectual regression. Epileptic convulsions occur. Eventually the child develops obvious involuntary movements of fine or gross choreiform, athetoid, or myoclonic character, with a striking tendency to rhythmicity. The child becomes progressively more stuporous, develops extrapyramidal symptoms, and finally reaches the end stage of spastic quadriplegia leading to death. The total course of the illness is usually less than twelve months, although many patients survive into the second year, and patients have been reported who survived eight and one-half[15] and nine[16] years.

Laboratory abnormalities are confined to the cerebrospinal fluid and the electroencephalogram. A first-zone colloidal gold curve is usually present at some time during the illness, and there is an elevation of the spinal fluid gamma globulin by electrophoresis.[17–20] Three distinct gamma globulin fractions may be identified.[21] Other studies of the cerebrospinal fluid are usually within normal limits, although a slight elevation

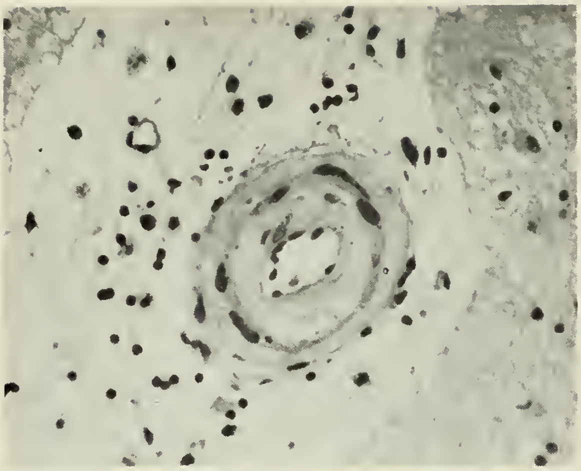

Fig. 5. Typical small artery in meninges with markedly thickened wall. Hematoxylin and eosin, × 400

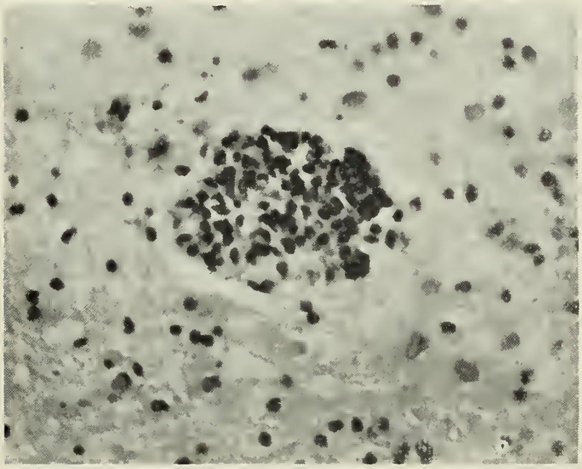

Fig. 6. Glial nodule and surrounding reactive astrocytes. Hematoxylin and eosin, × 400

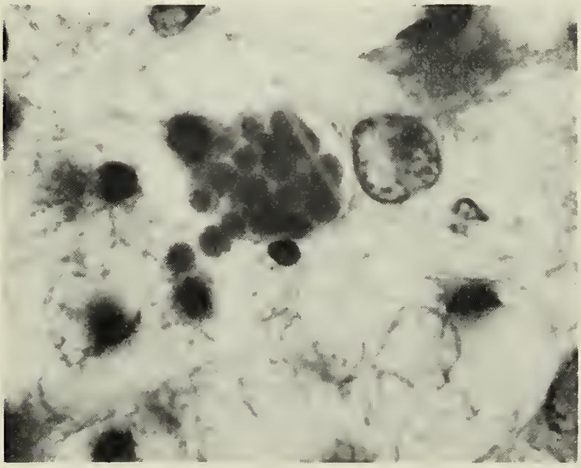

Fig. 7. Area of severe spongy degeneration containing Toxoplasma organisms. Phloxine B, × 1,200

of protein may be seen. The electroencephalographic pattern described by Radermecker[22] and Cobb and Hill,[23] while not pathognomonic of subacute sclerosing leukoencephalitis,[24] is considered diagnostic in combination with the above findings.[25] One sees the development of repetitive complex, high-voltage slow waves having a paroxysmal occurrence and a tendency to periodicity. With the eventual disappearance of normal rhythm, each complex of high-voltage slow wave is followed by a period of a few seconds of relative absence of activity from the record. On monopolar recording with occipital reference electrodes, Lorand and associates[26] noted the appearance of obligatory biphasic waves on the repetitive complexes with a positive component varying from 0.2 to 0.5 seconds and a negative component varying from 0.3 to 1.5 seconds in duration. In the final stage of the illness, the record may show absence of rhythmic activity.

Ocular changes such as papilledema and optic atrophy are known to occur frequently during the early or fairly advanced stages of subacute sclerosing leukoencephalitis.[27] Retinitis and macular degeneration also have been seen occasionally[15,28] and may occur early in the course of the illness.[29,30] Otradovec,[31] in a review of central chorioretinitis associated with subacute sclerosing leukoencephalitis, presented two interesting children who developed chorioretinitis three months before the onset of the first neurological symptom. One of the children had a negative complement-fixation test for toxoplasmosis. The evolution of these retinal lesions suggested to him an inflammatory process rather than a macular degeneration as seen with some of the storage diseases.

Toxoplasmosis may occur in the human being in either the congenital or the acquired forms. In the newborn infant, infection frequently results in a severe form of encephalomyelitis manifested by hydrocephalus, convulsions, spasticity of the extremities, and chorioretinitis.[32] Less commonly, the so-called acquired form of toxoplasmosis may also cause an encephalitis. In children, this is often a fulminating fatal illness, although recovery without sequelae may occur.[33–35] Systemic signs of parasitemia such as rash, lymphadenopathy, chorioretinitis, and splenomegaly are often present. Cerebrospinal fluid findings are usually normal but may reveal a pleocytosis, mainly of monocytes, with moderate elevation of protein. Specific reports in the literature of the electroencephalographic changes of toxoplasmic encephalitis are wanting. A study[36] of 32 patients with chorioretinitis and positive Sabin-Feldman dye tests revealed 73.4%

with some degree of abnormality in the electroencephalogram, consisting most frequently of paroxysmal sharp wave pattern, diffuse irregularity, and asymmetrical activity. Histologically, in the acquired form, small numbers of microglial nodules or necrotic areas are seen in the cerebral cortex, white matter, brainstem, or cervical cord. With appropriate stains, cysts of Toxoplasma organisms appearing as small eosinophilic bodies with pale blue cytoplasm may be seen within these areas or lying free in cells without any surrounding reaction. Calcifications develop in healed necrotic foci. There is frequent cuffing of vessels and sparse infiltration of the meninges with monocytes or polymorphonuclear cells.[33-35,37] Remington[38] relates the presence of cysts without a surrounding reaction to late stages of infection.

CONCLUSIONS

In consideration of the present case, there is little doubt of the diagnosis of toxoplasmic encephalitis. The development of chorioretinitis associated with a positive Sabin-Feldman dye test and the finding of numerous organisms in the brain at autopsy are conclusive. The evidence for the diagnosis of subacute sclerosing leukoencephalitis is also good. The clinical picture of a subacute course in a child involving personality change, convulsions, rhythmic involuntary dystonic movements, and neurological deterioration in association with an elevated first-zone colloidal gold curve and classical electroencephalographic changes are strongly suggestive. Tissue obtained from the brain biopsy performed one month before the appearance of the chorioretinitis revealed a picture compatible with subacute sclerosing leukoencephalitis with perivenous reaction, neuronal degeneration, and microglial proliferation.

A number of possibilities exist to explain the coincidental occurrence of these two diseases:

1] The child may indeed have had both subacute sclerosing leukoencephalitis and toxoplasmic encephalitis. [a] The toxoplasmosis was acquired during the course of the subacute encephalitis. A number of reported cases of fatal toxoplasmosis have occurred in patients with chronic diseases such as leukemia,[39,40] Hodgkin's disease,[41] and myeloid metaplasia.[42] In the report by Cheever and associates[43] of a patient with Hodgkin's disease, toxoplasmic organisms were found in the brain at postmortem examination, although toxoplasmin tests had been negative at the onset of the illness. [b] The subacute sclerosing leukoencephalitis reactivated a quiescent toxoplasmic focus of infection. It is known that children with apparent congenital toxoplasmosis may have no symptoms for several years.[44] On the other hand, O'Reilly[34] described the interesting case of a 9½-year-old girl who died of fulminating toxoplasmic encephalitis two and one-half years after an apparent parasitemia; during most of this interval she had been symptom-free. The presence of an evolving chorioretinitis occurring during the course of the illness in the case under discussion is more suggestive of an active parasitemia than a congenitally acquired infection.

2] The child may have had only one illness—toxoplasmic encephalitis. In a disease of unknown etiology such as subacute sclerosing leukoencephalitis, one must consider various agents. There are many features which both conditions have in common. In a child, toxoplasmosis complicated by encephalitis is usually an acute fulminating fatal illness, as noted earlier. In adults, however, a low-grade, self-limited infection may persist for many months.[37] In addition, either toxoplasmosis or subacute sclerosing leukoencephalitis may cause chorioretinitis. Rhythmic twitching of muscle groups such as the eyelids, the tongue, the face, or the extremities may occur in toxoplasmic encephalitis, presumably due to infiltration of the muscle with the parasite.[33,37] While descriptions of these movements do not suggest the more generalized pattern due to a central irritative focus as is seen in subacute sclerosing leukoencephalitis, conceivably identical areas of the brain could be involved, as evident from the known pathology. In either entity, microglial nodules may occur within the central nervous system. As pointed out by Ceballos,[45] the toxoplasmic organisms are easily missed and may pass for small lymphocytes or even inclusion bodies. With the routine Giemsa or Wright stains, cysts appear as clusters of small pink bodies with a pale blue halo. The inclusion bodies of subacute inclusion body encephalitis stain similarly, although located within the nucleus of either neurons or microglia, and have a homogenous appearance.

In conclusion, it must be said that in an entity which has received as much interest as subacute sclerosing leukoencephalitis with the frequent occurrence of inclusion bodies, it is inconceivable that toxoplasmic organisms could have been missed or confused with inclusion bodies in the majority of the cases. Whether or not the toxoplasmosis noted in the current case occurred as a complication or as an etiological agent remains unclear. Perhaps, as suggested by van Bogaert,[14] the characteristic clinical and pathological changes associated with subacute sclerosing leukoencephalitis represent a single mode of reaction of the nervous system, and these changes may be caused by various agents. It appears advisable in the future to consider the possibility of toxoplasmosis in cases of subacute sclerosing leukoencephalitis, especially when associated with chorioretinitis or other systemic symptoms suggestive of toxoplasmosis.

SUMMARY

A case of subacute sclerosing leukoencephalitis in association with toxoplasmic encephalitis is presented. Biopsy early in the course of the illness was suggestive of subacute sclerosing leukoencephalitis. Shortly afterward, the patient developed chorioretinitis, with rising dye titer for toxoplasmosis. At autopsy the brain revealed multiple cysts of Toxoplasma organisms in addition to cortical atrophy with extensive demyelination, glial nodules, and chronic inflammatory cells. The similarities between subacute sclerosing leukoencephalitis and toxoplasmosis are discussed, and the question is raised whether toxoplasmosis may be a causative agent of subacute sclerosing leukoencephalitis.

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A Survey of 156 Seizure Patients in a General Pediatric Clinic

ROSALIND S. ABERNATHY, M.D.
Little Rock, Arkansas

CHRONIC CONVULSIVE DISORDER or epilepsy begins in childhood in 90% of cases. Patients with recurrent convulsive seizures constitute a significant percentage of patients seen in any pediatric clinic.[1] The disease is chronic, attacks are of potential danger to the patient, and there is much popular fear and misunderstanding about the disease. Treatment of the patient involves the education of the parents about the nature of the illness and the necessity for prolonged, regular medication under continuous medical supervision. The physician's success in handling this chronic illness lies in his knowledge of the disease, familiarity with current therapy (primarily with drugs), and his ability to relate to the child and his parents over a long period of time.

Because of the apparent large number of children with chronic seizures attending the Pediatric Clinic at the University of Arkansas Medical Center, it was decided to review a sample of our patients in order to document the frequency of the illness, its nature as indicated by an evaluation of our patients, and our results with anticonvulsant therapy. A review of the literature revealed only 1 such study in children in the last twenty years.[2]

MATERIALS AND METHODS

During an eighteen-week-period, October 24, 1963, to February 26, 1964, 156 patients were seen at the University of Arkansas Medical Center with chronic recurrent convulsive seizures. Only patients on regular medication were selected for the study. The 156 charts were analyzed with respect to age, sex, race, and home county.

Evaluation of mental ability was made primarily on clinical grounds. Twenty-two children had had formal psychological testing, including testing before admission to special education classes. Mental ability was categorized as follows: [1] normal—all children making normal progress in school and those preschool children with normal developmental milestones and no objective evidence of slow development; [2] borderline—school children one grade behind or with very poor grades and preschool children with suggestive retardation; [3] retarded—children attending special education classes and of educable or high trainable level; and [4] very retarded—children in the low trainable or custodial level.

On the basis of past history and neurological examination, patients were divided into those with organic brain damage and those without. Criteria for inclusion in the organic brain damage group included a history of anoxia or damage at birth or during the neonatal period, brain abnormalities including microcephaly and hydrocephalus, and neurological abnormalities such as generalized spasticity or hemiplegias of any degree. Among the disease entities resulting in organic brain damage and epilepsy were bacterial meningitis, visceral larval migrans, kernicterus, DPT encephalitis, acquired aphasia, head injury, and cerebroretinal degeneration. Mental retardation without other findings was not considered a criteria for inclusion in the organic brain damage group. The two groups—brain damaged and nonorganic epileptic children—were analyzed for age of onset, mental ability, and degree of control. The death rate was noted.

Electroencephalographic results were classified as normal or abnormal and correlated with degree of control of seizures. No meaningful division of the children into seizure types could be made due to lack of uniformity in recording descriptions of their seizures. The overall impression was that more than 90% had generalized seizures resulting in loss of consciousness as at least part of their symptomatology and for which

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ROSALIND S. ABERNATHY *is assistant professor, Department of Pediatrics, University of Arkansas Medical Center, Little Rock.*

TABLE 1

Age	Seizure patients No.	%	Organic brain damage No.	%	Nonorganic No.	%	Organic/Total Ratio	% at each age of onset
0-6 months	21	13.5	16	32.7	5	4.7	16/21	76.2
6-24 months	45	28.8	13	26.5	32	29.9	13/45	28.9
2-4 yrs.	33	21.2	12	24.5	22	20.6	12/33	36.4
4-7 yrs.	25	16	3	6.1	22	20.6	3/25	12
More than 7 yrs.	32	20.5	5	10.2	26	24.3	5/32	15.6
Total	156	100	49	100	107	100		

TABLE 2

MENTAL ABILITY IN SEIZURE PATIENTS

			UAMC							
Groups	Keith[4] No.	%	Total No.	%	Organic brain damage No.	%	Nonorganic No.	%	Ratio organic/total	% at this mental level
Normal	142	48	69	44.2	6	12.2	63	58.9	6/69	8.7
Borderline	43	14.5	28	17.9	7	14.3	21	19.6	7/28	25
Retarded	111	37.5	36	23.1	15	30.6	21	19.6	15/36	21.7
Very retarded			23	14.7	21	42.9	2	1.9	21/23	91.3
Total	296	100	156	99.9	49	100	107	100		

they were treated. One small group of 8 patients with clear-cut petit mal staring spells was analyzed separately to compare with a recent study of the life history of petit mal.[3]

Fifteen months after the original selection of the patients, charts were again analyzed for the degree of control. Thirty-one patients had not been seen in the previous six months and no information had been obtained from the parents or public health nurses. For these patients, the control status was determined on the basis of information at their last clinic visit.

The remaining 125 patients could be classified into 5 groups: [1] *controlled, still on medication*—patients who had been free of seizures for one year, except for a girl with petit mal controlled for four months; [2] *controlled, off medication*—patients, most of whom had been controlled for at least two years while on medication; however, 5 had not relapsed after only two to ten months of treatment and may represent spontaneous remission; [3] *improved*—patients with either a marked decrease in the frequency of seizures or no seizures for four to eight months; [4] *relapsed*—patients previously controlled but having recurrence on treatment; and [5] *uncontrolled*—patients with no significant decrease in seizures.

Medication was recorded as to kinds of drugs and maximum daily dose and then analyzed for the controlling dose of medication. Toxic reactions to drugs were recorded as to type of reaction and the relationship of dose to symptoms.

RESULTS AND DISCUSSION

Incidence. During the eighteen-week period, 1,835 patients were seen in the pediatric clinic. Of these, 156 had chronic convulsive disorder or epilepsy. An additional 35 had this diagnosis considered, but were eliminated either because the diagnosis could not be established or another diagnosis was made, such as febrile seizure or a psychiatric disorder including hysterical or pseudoseizures. Thus, epilepsy was considered strongly in differential diagnosis of 10% of patients seen in our clinic and was the diagnosis in 8.5%.

Age, sex, and home county. At the time of the study, the patients ranged in age from 1 to 17 years. Seventy-five or 48% were less than 7 years of age and 81 or 52% were 7 or older. There was a slight preponderance of boys over girls—90 (58%) boys to 66 (42%) girls. This is almost exactly the ratio of the sexes reported by Keith[4] and Lennox.[5]

Eighty-six or 55% of the children were white and only 30% lived in Pulaski County where the medical center is located. This is in contrast with the general pediatric clinic in which 68% of the patients are Negro and 65% are from Pulaski County. The race and home county distribution suggests that the seizure patients are largely a referral group.

Age at onset of seizures (Table 1). The patients were distributed nearly equally in the 5 age ranges selected (0-6 months, 6-24 months, 2-4 years, 4-7 years, and over 7 years at onset). Thus, 80% had onset before 7 years of age. Livingston gives the most common age at onset of primary or nonorganic epilepsy as between 4 and 8 years.[1] This series, however, included patients considered to have organic brain damage, also called secondary epilepsy by Livingston,[1] symptomatic epilepsy by Chao,[6] or organic epilepsy by Lennox.[5] Exactly comparable figures are not available but since a large proportion of these patients have their organic brain damage as a result of developmental abnormalities of the brain or from birth injuries, it is logical that the onset of their seizures would occur early in life.

Mental ability (Table 2). Clinical estimation of mental ability indicates that roughly two-thirds of the patients are normal or borderline in intelligence, a finding remarkably close to the value obtained by Keith on a series of 296 patients studied at the Mayo Clinic.[4]

Two boys have shown definite mental deterioration during their course of uncontrollable seizures. One small girl has probably similarly deteriorated.

Case 1. A seven-year-old Negro girl walked at one year of age and was considered normal before surgery at 15 months for nonunion of a fractured right fibula. Her first grand mal seizure occurred two weeks after the operation. She had sporadic generalized seizures for eleven months, then developed frequent uncontrollable psychomotor seizures. At age 6, her I.Q. was estimated to be around 50.

Case 2. A white boy was making normal progress in school through the fifth grade. He failed sixth grade and dropped out of school the following year due to uncontrollable, very frequent myoclonic seizures and grand mal seizures every one to two weeks. At 16, he is functioning on a retarded level.

Case 3. Another white boy had an I.Q. of 115 in 1961 at age 10, although he had the behavior pattern and learning disabilities characteristic of the minimal brain dysfunction syndrome. He subsequently developed uncontrollable petit mal, psychomotor, and grand mal seizures. He made D and F grades in 1963, entered a special education class in the fall of 1964, and dropped out of school in the spring of 1965.

Organic brain damage with epilepsy and nonorganic or idiopathic epilepsy. By the criteria set down, 49 children were judged to have organic brain damage or 31.4% of the total. This is between Livingston's value of 36.5% of secondary epilepsy in his series of 4,158 children,[1] and Lennox's figure of 25.8% of 2,553 children.[5] In the United States, it is probably reasonable to expect that between one-third and one-fourth of chronic seizures are associated with organic brain damage. Fukuyama and associates, in contrast, have more symptomatic cases than idiopathic. Of their series, 422 of 801 patients (52.6%) were symptomatic.[2] Their criteria are somewhat broader since they included all mentally retarded patients and those with "severe character disturbances." It might also be postulated that the number of birth injuries and inadequately treated cases of meningitis is somewhat higher in Japan than in the U.S.A.

Among the children whose brain damage seems to have been acquired since the neonatal period were 5 cases of bacterial meningitis, occurring between 4 and 33 months of age, 4 of whom were treated in our hospital. Two were due to Hemophilus influenzae and no organism was recovered from the other 2. Two children developed unilateral seizures and, at the time of onset, were considered to have visceral larval migrans on the basis of a marked eosinophilia and serum precipitins to the Toxacara antigen. Two children had the diagnosis of cerebroretinal degeneration, 1 of the late infantile types of Bielschowsky and the other the juvenile form of Spielmeyer-Vogt.

Three deaths occurred in this series of 156 patients and all were in the organic brain damage group. One Negro male infant died at 15 months with kernicterus; the white male with the Bielschowsky's form of cerebroretinal degeneration died at 5½ years after a progressively downhill course. Another white male with microcephaly, generalized spasticity, and severe mental retardation died at 4½ years. All patients died at home and no autopsies were obtained.

As would be expected, the age at onset was younger for the organic brain damage patients (Table 1) and the percentage and degree of mental retardation was greater (Table 2). Control of seizures was less effective in the organic group (Table 4).

One hundred seven children or 68.7% of the total were considered to have nonorganic or idiopathic epilepsy. Although some of these are mentally retarded, percentage and severity of retardation are much less than in the organic group (Table 2), age of onset is somewhat later (Table 1), and degree of control was better (Table 4). Fukuyama and co-workers[2] found a slightly higher number of controlled patients (68.8%) in their nonorganic group and somewhat fewer controlled patients (38.8%) in the organic group.

EEG findings. One hundred forty of the 156 children studied had electroencephalograms and 42 had 2 or more. In 27 cases, the last or the only EEG was reported as normal, the other 113 were abnormal. Table 3 gives the degree of control for the children with normal and abnormal recordings. A normal EEG is generally considered a good prognostic sign and indicative of a more favorable response to medication.[6] This

TABLE 3

FINDINGS IN PETIT MAL EPILEPSY

	UAMC	*Holowach et al.*[3]
Total No. patients	8	88
Percent in total seizure patients	5.1%	5.6%
Age at onset	5½-11½ yrs.	80% between 2½-9 yrs.
Percent mentally retarded	37.5%	24%
Percent with other type seizures	75%	61%
EEG (3 sec. spike wave pattern)	75%	64%
Controlled on therapy	50%	62.5%
Sex ratio (M:F)	1:7	42:46

is supported by the values in Table 3. Fukuyama and associates show a similar trend with good control in 63% of patients with no spike discharge on EEG and 47.5% good control in those demonstrating a spike discharge.[2]

Petit mal seizures (Table 3). One small group of 8 patients with petit mal staring spells was selected for special analysis in order to compare the findings with those of Holowach and associates from Washington University.[3] The results are quite similar with respect to the incidence of petit mal, the percentage of mental retardation, the number of children with other types of seizures, and the difficulty of achieving control of petit mal staring spells. The age of onset of the Arkansas group is slightly older than in the Washington University group. Only in the proportion of girls to boys does our group show the more classical finding of a preponderance of girls (1, 5) in contrast to the findings of Holowach and co-workers.[3]

In one of our uncontrolled patients, no attempt was made to control her petit mal seizures because of inadequate observation and lack of cooperation of the parents. Another patient with uncontrolled petit mal seizures has failed to return for further adjustment in medication.

The 4 controlled patients were all taking phenobarbital; 3 were also taking trimethadione (Tridione®) and the fourth ethosuximide (Zarontin®).

The findings of Washington University and the UAMC with respect to control of petit mal seizures is in contrast to those of Fukuyama who had his best results with petit mal. Twenty-five of 801 or 3% of his patients had this diagnosis. Eighty-eight percent were well controlled, primarily on Tridione®.[2]

Control of seizures with anticonvulsive medication (Table 4). Analysis of the state of control of the 125 patients heard from within the last six months is shown in Table 3. Seventy-one patients were controlled; 18 were improved or had relapsed after good control. Only 36 or 29% were uncontrolled.

Of the 8 patients who relapsed after good control, 3 had recurrences after being seizure free from twenty-two to twenty-six months and all 3 were still taking medication. The other 5 relapses seemed to be related to dosage changes, as follows:

1] A 9-year-old white boy was controlled for one year with diphenylhydantoin (Dilantin®) but had a recurrence when he began to take his medication irregularly.

2] A 2-year-old Negro boy was controlled for one year on phenobarbital. His dose was reduced by a clinic physician and he had a recurrence.

3] A 12½-year-old Negro girl was seizure free for fifteen months on phenobarbital and Dilantin®. Phenobarbital was discontinued and seizures recurred.

TABLE 4

CONTROL OF SEIZURES

	Total group		*No recent information*		*Organic*		*Nonorganic*		*Normal EEG*		*Abnormal EEG*	
Groups	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Total controlled	71	56.8	7	25	17	45.9	55	62.5	16	72.7	49	53.8
A—controlled still on medication	44	35.2										
B—controlled and off medication	27	21.6										
Improved	10	8	8	28.6	1	2.7	9	10.2	2	9.1	8	8.8
Relapsed	8	6.4	2	7.1	2	5.4	6	6.8	1	4.5	6	6.6
Uncontrolled	36	28.8	11	39.3	17	45.9	18	20.5	3	13.6	28	30.8
Total	125	100	28	100	37	99.9	88	100	22	99.9	91	100
Unable to evaluate	31		3		12		19		5		22	
Total	156		31		49		107		27		113	

4] An 8-year-old white boy was taken off phenobarbital and Dilantin® after it was thought he had been seizure free for two years. Actually, his last seizure had been thirteen months before. Another seizure occurred.

5] A 7-year-old white boy was being treated for akinetic seizures with phenobarbital without noticable response. Tridione® was added and control achieved. Phenobarbital was then stopped and his akinetic seizures recurred.

An analysis of the patients on whom there is no recent information, based on their status at the last clinic visit, is also presented in Table 4. The 7 patients presumed to be controlled had been seizure-free for from thirteen months to seven years at their last clinic visit. The 8 improved patients had been controlled for one to eleven months at their last visit. Two had relapsed after eleven months and four years of control, respectively. Three had never returned after the initial visit.

The 36 uncontrolled patients included 9 who took their medication irregularly. It may be speculated that with better cooperation, these patients might have had their seizures controlled.

MEDICATION

Total usage. Although 13 different anticonvulsive drugs were used in the treatment of these patients, phenobarbital and Dilantin® were used most commonly, with Tridione® next. One hundred fifty-two or 97% of the children were on phenobarbital at some time. Seventy-eight or 50% used Dilantin® and 23 or 15% were taking Tridione® at some time. Sixty-nine children took phenobarbital alone, 1 Dilantin® only, and 47 phenobarbital and Dilantin® only. Thus, 117 or 75% were treated with only these two drugs.

Medication in controlled patients. The records of the 71 children whose seizures were considered to be controlled plus the 7 with presumably controlled seizures were analyzed for drug usage. Seventy or 90% of these patients were controlled on phenobarbital and Dilantin®. Forty-eight were controlled on phenobarbital alone, 4 on Dilantin® alone, and the remaining 18 on the combination of the 2 drugs. It is interesting to note that among 425 well-controlled patients in Fukuyama's series from Tokyo, 93% were on phenobarbital and 90% on Dilantin®.[2]

The remaining 8 controlled patients were on 7 different combinations of drugs. Two were on phenobarbital, Dilantin®, and Tridione®. The other 6 combinations were phenobarbital and Tridione®; phenobarbital and primidone (Mysoline®); phenobarbital and acetazolamide (Diamox®); phenobarbital, Diamox®, and Zarontin®; phenobarbital and Zarontin®; and Dilantin® and Zarontin®.

Quantitative dose levels. The average controlling dose of phenobarbital in the 48 patients controlled on this drug was 4.5 mg. per kilogram with a range of 2 to 10 mg. per kilogram. For 8 older children, aged 10 to 15 years, the dose was lower, ranging from 2.3 to 4.1 mg. per kilogram with an average of 2.8 mg. per kilogram. Twenty-two children were controlled on Dilantin® alone or Dilantin® with phenobarbital. In 2 cases there is considerable doubt as to whether the medication did in fact control the seizures. One infant had uncontrollable seizures from birth to 14 months when he went into remission, probably unrelated to his dose of Dilantin® of 15 mg. per kilogram. Another very large adolescent girl was taking only 1.2 mg. per kilogram of Dilantin® and remained on the drug for only a short period of time. Seizures did not recur. The average dose of the remaining 20 patients was 6 mg. per kilogram with a range of 4 to 10 mg. per kilogram.

Fukuyama and co-worker's data on effective dosages of Dilantin® are very similar to those of this study. For children between 2 and 10 years of age, the dose range was between 4 and 9 mg. per kilogram. A somewhat lower dose (4-6 mg. per kilogram) was found effective for children more than 11 years of age. The Japanese authors do not calculate the phenobarbital dosage by weight but the actual dose level of 0.05 to 0.1 gm. per day seems considerably lower than that taken by many of our patients. Fukuyama implies that higher doses of phenobarbital are accompanied by unpleasant side effects. His restricted dose of phenobarbital may account for the fact that, while in both studies, 93% of the controlled patients were on phenobarbital, Dilantin® was used in only 32% of the controlled UAMC cases while 90% of the Japanese children were taking it.

The 3 children, ages 7 to 10, whose controlling medication included Tridione®, were taking 23, 30, and 30 mg. per kilogram, respectively. Three children, ages 9 to 13, controlled on Zarontin®, were taking 14, 14, and 28 mg. per kilogram, respectively.

Diamox® with phenobarbital achieved good control at a dose of 25 mg. per kilogram for a 5-year-old boy who had been having up to 25 myoclonic seizures a day after a head injury. A 9-year-old boy, controlled on 3 drugs, was taking Diamox® at a dose of 18 mg. per kilogram.

Toxicity from medication (Table 5). Not only was phenobarbital the most commonly used drug

TABLE 5

TOXICITY RELATED TO DOSE IN PHENOBARBITAL (6 pts.) AND DILANTIN® (6 pts.)

	Phenobarbital (mg./kg.)		*Dilantin® (mg./kg.)*	
	Average dose	*Range*	*Average dose*	*Range*
Symptoms	6.2	4-8	12.4	10.5-14
No symptoms	3.2	2-4	6.6	4-9

but it also produced the fewest toxic reactions. Nine percent of the 152 patients taking phenobarbital had some toxicity. Excluding the nearly universal symptom of gum hypertrophy in the 78 children on Dilantin®, 20% showed toxicity, while 30% of the 23 patients on Tridione® had symptoms.

Only 5 children were discontinued on phenobarbital permanently because of reactions. Rashes were noted in 2 children, one of whom also suffered from an increase in hyperactivity while on the drug. Three others were taken off because of drowsiness and other associated symptoms. Six children, who were drowsy on larger doses of phenobarbital, tolerated a lower dose. Two suffered acute accidental overdosage of phenobarbital. One had two such episodes.

Toxic reactions to Dilantin® were twice as frequent as reactions to phenobarbital. All patients had gum hypertrophy. One had severe hirsutism. There were 4 severe episodes of ataxia due to an excessive dose of hydantoin drug. In 3 cases, Dilantin® was administered at a dose of 22 to 27 mg. per kilogram. The fourth case was that of a mentally retarded boy with akinetic seizures, poorly controlled on Dilantin® prescribed in our clinic. An outside physician added a full dose of phenantoin (Mesantoin®) to this. The boy soon became very drowsy and ataxic, and his grandmother stopped all medication, which precipitated a series of 13 grand mal seizures within four days. These four acutely intoxicated patients later tolerated doses of Dilantin® of 6 to 9 mg. per kilogram. Six patients could not tolerate Dilantin® without ataxia, even in more modest doses (7 to 15 mg.) and had to be taken off the drug. Six others were ataxic at higher doses but tolerated lower doses well.

No patients showed any hematologic or renal complications from Tridione.® Seven children did develop symptoms and all were taken off the drug. Two children were noted to have an increased number of seizures on Tridione.® One of these also developed a rash. Rash alone was the complaint of another child. Drowsiness was noted in 2, associated with blurred vision in one case. There was one complaint each of vomiting and crying spells while on Tridione®.

SUMMARY AND CONCLUSIONS

This study of 156 patients illustrates that convulsive disorders constitute a significant proportion of patients seen in a general pediatric outpatient department.

More than 60% of the patients were judged to be of normal or borderline mental ability. About one-third showed objective signs of organic brain damage. These children had an earlier onset of seizures, poorer control, and more mental retardation, often of a severe degree. Three deaths occurred in the series, all in the organic brain damage group.

A review of 8 cases of petit mal epilepsy indicates a preponderance of girls with this affliction but a prognosis no different than for other types of seizures.

Seventy percent of the patients became seizure free or significantly improved on therapy. Of the 29% of the patients whose seizures were uncontrolled, one-fourth did not take their medication regularly.

It has been the policy in the UAMC Pediatric Clinic, since 1961, to treat all seizure patients with phenobarbital initially and to add Dilantin® if adequate seizure control cannot be obtained with nontoxic doses of phenobarbital. Since 90% of the fully controlled patients were on one or the other of these drugs or in combination, this seems to have been a wise policy. Phenobarbital is low in toxicity and much the lowest in cost of the popular anticonvulsive drugs. Dilantin® ranks second in toxicity and cost. Ten percent of the controlled patients required combinations of other drugs and 29% are as yet uncontrolled.

The majority of children with seizures can probably be handled adequately in a general pediatric clinic which is well oriented to the care of seizure patients. A pediatric neurology or special seizure clinic is the ideal place to manage the more difficult problems.

We have been fortunate to have an active Pediatric Neurology Clinic directed by Dr. John Bornhofen since the beginning of this study. This clinic has handled our difficult cases.

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The Child with Minimal Brain Dysfunction

A Multidisciplinary Catalyst

SAM D. CLEMENTS, Ph.D.
Little Rock, Arkansas

THE CHILD with the medical diagnosis of minimal brain dysfunction (or the educational diagnosis of "specific learning disabilities") is the current focus of unprecedented multidisciplinary interest and concern. Such children are serving as apparent catalysts for collaborative diagnostic and therapeutic efforts among pediatricians, child psychologists, educators, pediatric neurologists, language pathologists, and child psychiatrists.

Since minimal dysfunctioning of the central nervous system is believed to affect such a large number of children (estimates range from 5 to 20% of the general school population) and since the condition is basically a form of physical handicap, that is, mild neurologic impairment manifesting as deviations in learning and behavior, it is only logical that these children have become of major importance to the entire health field.

Perhaps the most significant outcome of this situation has been the development of many new and useful approaches and techniques in the general field of child guidance. The pediatrician or general practitioner who might have felt insufficiently prepared and, therefore, hesitant to trespass into the territory of the mental and emotional aspects of children is now being trained to recognize such youngsters as they come through the private practice office or the specialized child study clinic. The happy result has been a more realistic meaning for the concepts of the "whole child" and the "new pediatrics." In the past, these two doctrines have been more preached than practiced.

On superficial examination of the child with minimal brain dysfunctioning, the listing of differential diagnoses might include the following: [1] mental subnormality, [2] emotional disturbance, [3] visual impairment, [4] auditory impairment, [5] mild brain damage, and [6] motor coordination impairment, and so forth.

In a sense, the child will display some of the symptoms usually associated with all these conditions. Following is a list of the outstanding characteristics associated with the syndromes of minimal brain dysfunctioning in children.

1] *Specific learning disabilities* are most common in the basic academic skills of reading, arithmetic, and spelling; the child may have difficulty with such abstract concepts as time and space and in mastering tasks which are dependent upon intact integration and functioning of the visual-motor-perceptual systems. The specificity of the deficits in learning is the major factor here, since individual and comprehensive assessment of intellectual functioning will indicate average or above capacity and potential.

2] *Perceptual-motor deficits.* These include poor printing, writing, and drawing; inferior, erratic, and immature performance when reproducing geometric figures from design cards (Bender Visual Motor Gestalt test); and difficulty with figure-ground or whole-part discriminations, or both.

3] *General coordination deficits.* The child may frequently be described as awkward or clumsy. This may appear in either fine muscle performances or in overall coordination, or both.

4] *Abnormal activity level.* If hyperkinetic, the child appears to be in constant motion, flitting from one object or activity to another, or he may be merely restless and fidgety. The child's "organic drivenness" may also manifest as voluble, uninhibited speech or as disorganized thought processes, even in the absence of outward hyperactivity.

On the other hand, the hypokinetic child is described as "slow as molasses" or "daydreamy," since he moves, thinks, and talks at a diminished

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SAM D. CLEMENTS *is associate professor, departments of pediatrics and psychiatry, and director, Child Guidance Study Unit, University of Arkansas Medical Center, Little Rock.*

rate. Frequently, this slow responding child will have an "aphasic" quality in his speech productions.

5] *Impulsivity.* The child cannot keep from touching and handling objects, particularly in a strange or overstimulating environment. He frequently speaks out without checking himself; he may curse, be insulting, or eagerly blurt out all the family secrets. Such impulsivity easily leads him into conflict with the demands of conformity as established by family, school, and society. Some children may commit striking antisocial acts such as stealing, fire setting, and so forth, with only a modicum of provocation and with apparent inability to foresee the consequences.

6] *Emotional lability.* The child may be described as irritable, "high-strung," aggressive, or easily moved to tears; he may have quick changes of emotional behavior from high temper to remorse and easy manageability. The above characteristics are usually ascribed to the hyperkinetic child. The hypokinetic child, on the other hand, is usually pleasant and even tempered, cooperative, and diligent and displays a high tolerance for academic frustration and failure.

7] *Short attention span or distractibility, or both.* The child is unable to concentrate on one activity for the length of time appropriate for his age and is easily distracted by casual stimuli.

8] *"Soft" or equivocal neurological signs.* Careful neurological examinations conducted on child guidance populations indicate that the most frequently seen of such signs are transient strabismus; dysdiadochokinesis; poor coordination of fingers; mixed or confused laterality, or both; impaired visual or auditory perceptual systems, or both; disorder of speech or a history of slow speech development or irregularity; hyper- or hypokinesis; and general motor awkwardness.

9] *Electroencephalographic irregularities.* Although agreement is not complete in this area, the high frequency of borderline or abnormal brain wave test records is significant.

It is important to emphasize that a given child may not have symptoms in all or even many of these areas, since each child presents his own particular cluster of symptoms. The level of his native intellectual capacity and the nature of his underlying temperament will determine the form and the manner and means of compensation for the deficits or deviations. The result is a variety of syndromes contained within the primary diagnosis of minimal brain dysfunctioning. Certain symptoms do cluster to form recognizable clinical entities. The "hyperkinetic syndrome" is perhaps the most obvious example. Others include "primary reading disability," "the hypokinetic syndrome," and various forms of the aphasias.

A multidisciplinary approach to diagnosis and therapy is deemed essential to provide maximal benefit for the child and his parents. Child guidance can no longer be restricted to the traditional team comprised of clinical psychologist, psychiatric social worker, and psychiatrist. A full complement of specialists is required to provide a useful and comprehensive evaluation of the deviating child. In addition to the social worker, psychologist, and psychiatrist, the new team must now include a pediatrician, a pediatric neurologist, an educational diagnostician, a language pathologist, and, ideally, an occupational and physical therapist.

Such a large-scale team operation is seldom found working together within a single facility. It is perhaps most closely approximated in a medical center setting or in the very large community or state-operated child centers.

DIAGNOSTIC PROCEDURES

Unfortunately, an endless variety of factors can influence the final diagnosis of a child and, often, of his parents. These include the disciplines of the diagnosticians as well as the training, experience, and attitudes they bring with them into the diagnostic evaluation procedure; the diagnostic setting, that is, the medical center or community mental health clinic, and, most important, the diagnostic procedure itself, particularly in terms of time, number, and variety of measures obtained; and the use of a uni- or multidisciplinary approach. The major failure of child guidance is the fact that no standardized and routine diagnostic procedure has yet been constructed that would be used by all facilities involved in the diagnosis of deviant children. The guidelines for such a diagnostic procedure must include the following: [1] histories, including medical, developmental, family-social, and academic, [2] pediatric physical examination, including assessment of general physical status and a detailed neurologic examination, [3] special examinations, including ophthalmologic and otologic examinations as well as electroencephalographic studies, [4] psychological evaluation, including individual comprehensive assessment of intellectual functioning, measures of complex visual-motor-perceptual integration and functioning, behavioral observations in a variety of settings, and so forth, [5] language evaluation, including the expressive and receptive aspects of speech and language behavior, and [6] educational evaluation, including analyses of academic abilities in reading, number concepts, and so forth.

TREATMENT AND MANAGEMENT PROCEDURES

The treatment plan for the child with minimal brain dysfunction must include the areas of interpretation to and counseling of the parents, home management for the child, educational planning for the child, and possible medication for the child.

Once the diagnosis has been confirmed by the evaluation team, the parents are given an "organic" interpretation of the learning or behavior problems, or both, of their child. Both parents are required to be present for this conference. The relief they feel and the lessening of guilt associated with the possibility of being "bad" parents pave the way for better understanding of the child's condition and generate a more useful set of attitudes in their management of him.

Home management includes the provision of a more routinized and scheduled program for the child, a decrease in environmental stimulation, and consistency between parents in the handling of problems of discipline, that is, a minimal amount of verbal bargaining with the child but rather clear, firm, and precise statements of behavioral expectations and limits. These, and other aspects of home management styled to the uniqueness of the particular family, plus the knowledge that many of the child's more irritating symptoms such as hyperactivity, poor school achievement, short attention span, and so forth, are really beyond the child's control, do much to improve the general home atmosphere.

Proper educational management is perhaps the most important and often the most difficult part of the therapeutic program to arrange. Close cooperation with the diagnostic team and the school administrators and teachers is mandatory. The school system through its special educational program may be able to provide the kind of specialized training and experience the child will need. Many states now provide visual and auditory perceptual training for children with minimal brain dysfunctioning in their public school systems. Parochial and other private schools are also adding this service to their regular programs. It may be necessary to find a tutor to work with the child on reading, arithmetic, and so forth, in addition to his regular school program. Some child guidance clinics now provide academic remedial service through the addition of an educational therapist to their regular staff. Academic intervention must be made as early as possible in the child's school career. Otherwise, his difficulties can become compounded by repeated failure and frustration.

Proper medication is seen as a very important adjunct to the total treatment plan. The following medications have been found most helpful in reducing hyperactivity and irritability and in increasing attention span: captodiamine hydrochloride (Suvren®), thioridazine hydrochloride (Mellaril®), and the amphetamines [dextroamphetamine sulfate (Dexedrine®) and amphetamine sulfate (Benzedrine®)]. Since children vary in their response to the various drugs and dosages, there is often the necessity of a period of experimentation to attain the most useful prescription for a given child. After the drug is regulated, the child should be seen at three-month intervals for blood studies and additional planning.

Most clinics report marked and immediate improvement of the children on a regimen of medication, special teaching, and infrequent counseling of parents. This fact is very important in replying to the frequent complaint that child guidance clinics tend to bog down with a few "intensive" psychotherapy cases and cannot provide service to even a small portion of the public who seeks it. The community stands to gain by the utilization of all methods which show success in dealing with deviant children.

The child with minimal brain dysfunctioning has provided long-needed fresh considerations in the areas of pathology, diagnosis, treatment, education, and investigation of children with learning and behavior disorders. Concern for this large group of handicapped children has had a positive influence on the use and usefulness of a collaborative approach.

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Immune Mechanisms in Disease

VIDA H. GORDON, M.D.

Little Rock, Arkansas

AN IMMUNE RESPONSE indicates the production of antibodies and the resulting state of immunity or hypersensitivity in the response of the host to an antigen. Ordinarily we think of immunity as indicating protection or resistance against disease because of the presence of specific antibodies. However, hypersensitivity indicates production of a disease because of the presence of antibody and antigen in a susceptible shock organ.[1]

There is a wide variety of substances that may stimulate an immune response with the formation of a specific antibody in the host animal. These substances are [1] proteins, including bacteria, [2] polysaccharides, especially ones of high molecular weight, and [3] synthetic polymers such as dextrans. The antigenicity of lipids is less certain, but they probably are not complete antigens and are antigenic primarily when combined with proteins or polysaccharides.[1,2]

Simple chemical substances, such as certain drugs, have the capacity to react with antibodies.[3] They can also act as incomplete antigens or haptenes and stimulate antibody formation when they are coupled to a larger carrier molecule, such as the protein of the body tissue of the host[4] (Fig. 1).

ANTIGENS

Ordinarily, strong antigens are of a molecular weight of over 40,000. We do know that antigenicity tends to increase with an increase in the size of the molecule. The material which is antigenic for the animal must be "foreign" to the animal and not recognized by the host itself. Contrary to earlier opinion, immunologic specificity of an antigen is not governed by a small determinant section of the protein, namely, an aromatic group. We cannot state positively what gives antigenic specificity, but we do know that the order of amino acids in the peptide chain affects its specificity.[1] An antigenic molecule of only moderate size can combine with several molecules of antibody. This shows that the portion of the antigenic surface toward which the antibody is directed is usually part of the whole molecule.

ANTIBODIES

Antibodies formed to one determinant group, although related, are not entirely identical, but, as evident from their cross-reactions with heterologous antigens, they vary to some extent around a main pattern. What ordinarily is spoken of as an antibody is generally a mixture of specifically different components.[5]

In the antibody population induced against a single antigen determinant, there will be a range of affinities with which the antibody molecules will complex with homologous antigen. This heterogenicity appears to be a phenomenon unique to the immune response, since it does not apply to the behavior of enzymes in the formation of complexes with their substrate molecules.[5]

Antibodies are modified asymmetrical globulin molecules formed as a result of antigenic stimulation. They react specifically with that antigen. The molecular weight of antibody protein ranges from 160,000 for gamma globulin to 1,000,000 for macroglobulin. It was thought for some time that isoagglutinins were an exception to this, but now it is believed that anti-A and anti-B are immune antibodies as most other agglutinins and that they are found in response to antigens in food, bacteria, or animal parasites which are chemically similar to the A and B antigens of man. Isoagglutinins usually appear in the serum about the second month of life.[6] By electrophoresis, antibodies can be identified in those fractions of serum called gamma$_2$ and occasionally in gamma$_1$, beta, and alpha globulins. Figure 2 is an attempt to bring together the various categories by which these serum fractions may be designated, inasmuch as the terminology is very confusing in the literature when different names refer to the same fraction.[7–10] A com-

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VIDA H. GORDON *is associate professor, Departments of Pediatrics and Microbiology, University of Arkansas Medical Center, Little Rock.*

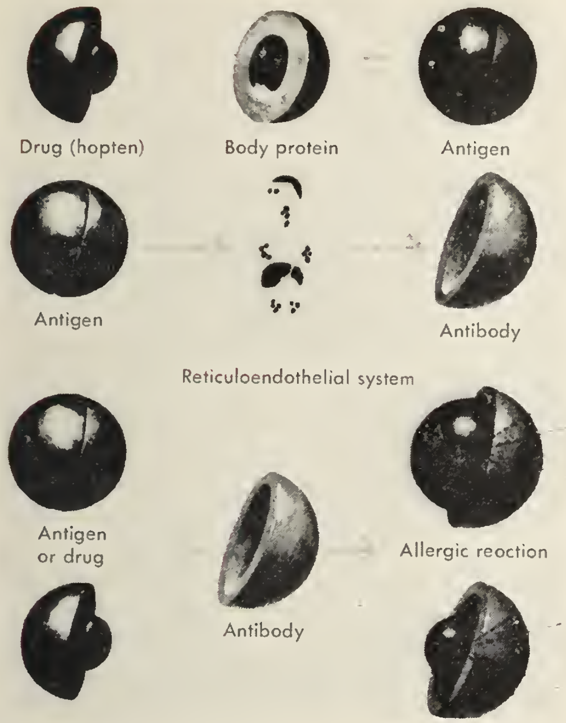
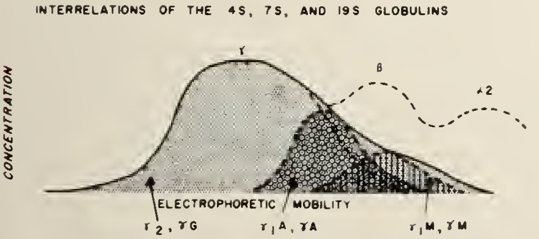


Fig. 1. Ability of drug to act as an antigen, by itself or combined with body protein

mittee of the World Health Organization, meeting in 1964, proposed as the preferred terminology gamma G for $gamma_2$, gamma A for B_2A, and gamma M for B_2M. The 7S gamma fraction contains the antitoxins and the antibacterial and antiviral antibodies. $Beta_2A$ has been found to be the site of atopic antibody and probably some others.[9,11] $Beta_2M$ contains the natural isohemagglutinins, heterophil antibodies, rheumatoid factor, cold agglutinins, Wassermann antibody, and antibody to the O antigen of the gram-negative bacillus. Most evidence, as yet not conclusive, suggests the following genesis of antibody.



	γ_2, γG	γ_1A, γA	γ_1M, γM
SYNONYMS	γ, 7S	βx, β_2A	γ1, 19Sγ, β_2M β_2 macroglobulin
EP MOBILITY	range from γ - α_2	γ → β	β → α 2
MOL. WEIGHT	160,000	±160,000	1,000,000
SOURCE	PLASMA CELL	PLASMA CELL	LYMPHOCYTE AND ? PLASMA CELL PROBABLY IN SPLEEN
PERCENT OF TOTAL	75%	15 %	10 %
PLACENTAL PASSAGE	YES	NO	NO

Fig. 2. Immunoglobulins of normal human serum, with differentiating features of three major fractions[7-10]

Evidence for role of lymphocytes in antibody formation. Lymphocytes play an important role in antibody formation.[1] Lymphocytes obtained from immunized animals injected into irradiated recipients transfer antibody capacity. Dixon[12] and others[13,14] have shown that lymphocytes under antigenic stimulation can become plasma cells. He immunized rabbits with bovine serum albumen (BSA) and transferred the lymphocytes from these rabbits into the subcutaneous space of rabbits proved to be immunologically impotent. He then injected BSA. When examined at biopsy, the lymphocytes had changed into plasma cells. Antibody molecules in these cells were stained with Coons' fluorescent technique so that they could be identified.

Evidence for role of plasma cells in antibody formation. There is ample evidence that plasma cells play an important role in antibody formation: [1] Agammaglobulinemia patients, in whom circulating antibodies are absent, do not have plasma cells.[15] [2] Lymph nodes in hyperimmunized children, or those immunized recently, are rich in plasma cells.[16] [3] Certain instances of drug hypersensitivity are associated with an increase in plasma cells, even in the bone marrow. [4] Several diseases suspected as most likely to have a hypersensitivity etiology are associated with an increase in plasma cells, such as serum sickness, hypergammaglobulinemia, which is usually associated with plasmacytosis, systemic lupus erythematosus, and even rheumatoid arthritis.

TYPES OF ANTIBODIES

There are many different kinds of circulating antibodies: [1] the precipitating or so-called classical antibody (Ab), [2] the nonprecipitating, skin-sensitizing antibody or reagin, and [3] the nonprecipitating, nonskin-sensitizing antibody or blocking antibody, which can be induced by multiple injections of an antigen.

METABOLISM OF ANTIBODY AND ANTIGEN

Plasma proteins normally exist in dynamic equilibrium almost equally divided between intra- and extravascular compartments of the plasma pool. I^{131}-labeled homologous proteins injected intravenously rapidly equilibrate within this pool, with a resultant abrupt drop in their circulating concentrations to about one-half the initial value in one day.[17] After the initial equilibration,

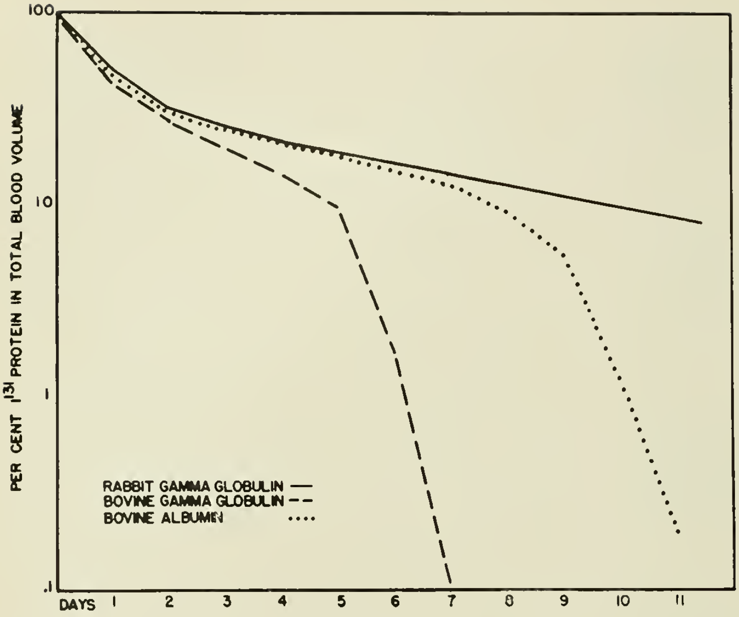


Fig. 3. Disappearance of I^{131} proteins from the blood of rabbits. Percentage of I^{131} protein in total blood volume is plotted logarithmically against time after injection[18]

they are lost as a result of catabolism at a logarithmic rate characteristic of the species.

Metabolism of antigen and antibody gives an insight into the character of the immune response.[18] Most of the work that has been done on the nature of the immune response has concentrated on either the fate of antigen or the production of antibody, with few attempts to study both sides of this immunologic coin in the system. In order to have an antigen relatively pure and readily catabolized by the host, so that complications resulting from undue persistence of antigen in the host would be minimized, Dixon used fractionated serum protein antigens trace-labeled with radioactive I^{131}. The host in these experiments was the rabbit. In Figure 3 the plasma level of I^{131}-labeled homologous gamma globulin injected into rabbits is shown by the solid line. After initial equilibrium, homologous rabbit gamma globulin is lost at an exponential rate with a half-life of five days. Heterologous proteins also equilibrate within the plasma protein pool as shown by the two examples—I^{131}-labeled bovine serum albumin (I*BSA), dotted line, and I^{131}-labeled bovine gamma globulin (I*BGG), dashed line. As part of the protein

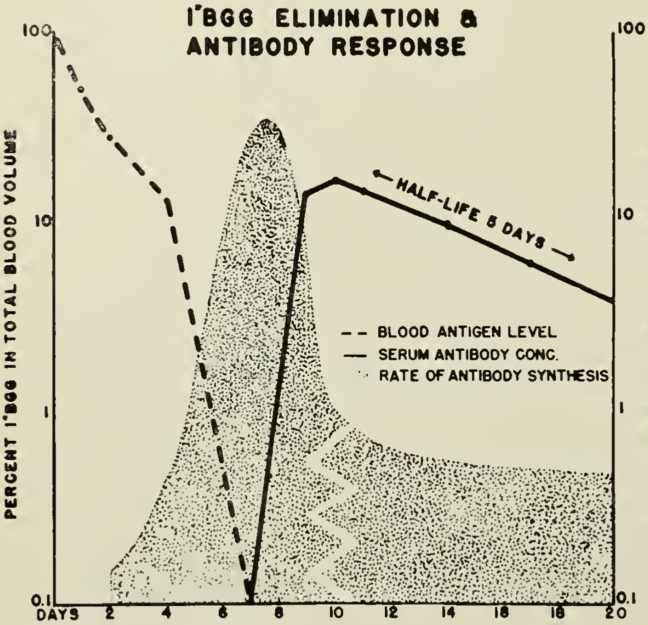


Fig. 4. Estimated rate of antibody synthesis in primary response superimposed on lines representing serum antigen elimination and antibody response[18,19]

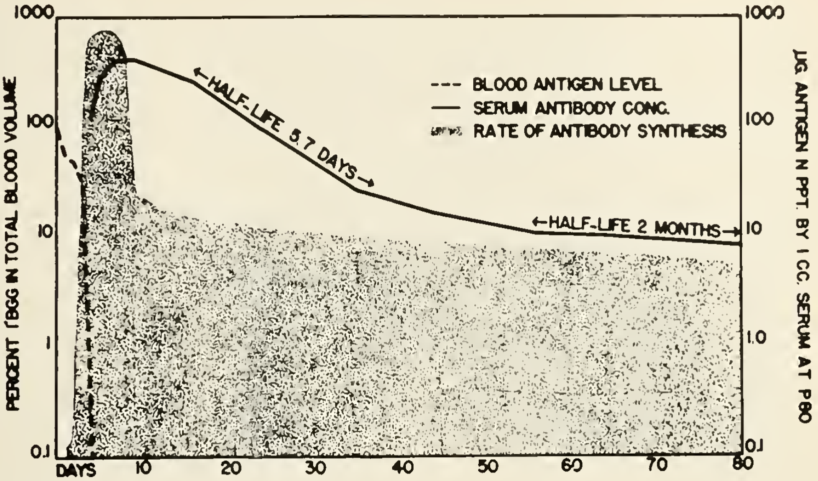


Fig. 5. Serum concentrations of antigen and estimated rate of antibody synthesis in specific anamnestic response to I*BGG[18]

plasma pool, these antigens are in intimate contact with all the tissues of the host.

I*BSA is catabolized at the same rate as is the homologous protein for seven days. After that time, rapid elimination of I*BSA from the circulation indicates an increased rate of catabolism as a result of the appearance of antibody.

In the case of I*BGG, equilibration occurs and then the rapid antibody-induced catabolism begins, only three or four days after the injection. Apparently, as antibody appears in the presence of circulating antigen, antigen-antibody complexes are formed, picked up by fixed and circulating phagocytic cells, and then rapidly catabolized.

Primary response. The amount of free antibody appearing in the serum in the primary response to I*BGG (30 mg. per kilogram) is shown in Figure 4.[18,19] Antigen elimination is indicated by the dashed line and serum antibody by the solid line. Immediately after the elimination of detectable circulating antigen, the level of antibody in the serum rises rapidly to a maximum value within three days. Following this, the serum antibody concentration declines at a logarithmic rate with a half-life of five days.

The rate of antibody synthesis is indicated by the shaded area. It starts on about the second or third day after the injection, when the rate of antigen elimination is increased, and reaches a maximum about the time of disappearance of antigen. It then falls to levels a few percent of the maximum rate of synthesis, prior to the time of maximum serum antibody concentration. The shaded area to the right of the zigzag line indicates the maximum amount of persistent antibody synthesis observed in any of the animals.

Anamnestic response. In the anamnestic response or so-called booster, however, as these experimental results show, the phase of immune elimination of circulating antigen from the blood is completed within four days, shown by the dotted line in Figure 5. Then for twenty days there is a fall of antibody level at a rate with a half-life of about 5.7 days. Finally, the decline in serum antibody concentration slows and approaches a rate with a half-life of more than two months.[18]

The shaded area shows the rate of antibody synthesis. It is evident that the rate is rapid at first and for a short time after the antigen is detected in the serum. About five days after the booster injection, however, there is a rapid fall and a decrease logarithmically, with a half-life of two months. This accounts for the slow rate of serum antibody decline in the next six or seven months. Whether or not antibody synthesis continues at this basal rate in the absence of antigen cannot be decided definitely by tracer techniques. It is apparent that rapid synthesis of antibody occurs only during, and perhaps for a short time after, the time when the antigen is definitely detectable in the host.

During the decline of serum antibody concentration in the anamnestic response, the half-life of the homologous gamma globulin, as opposed to the heterologous, remains normal, or five to seven days, indicating that continued antibody synthesis, not slowed catabolism, is responsible for the slow antibody decline. The rate of homologous gamma globulin metabolism varies considerably from species to species and inversely with the metabolic rate of the host expressed in unit weight.

The slower gamma globulin catabolism in children than in adults might be related to the lower metabolic rate during the early months of life, in addition to other unknown factors.[18] To

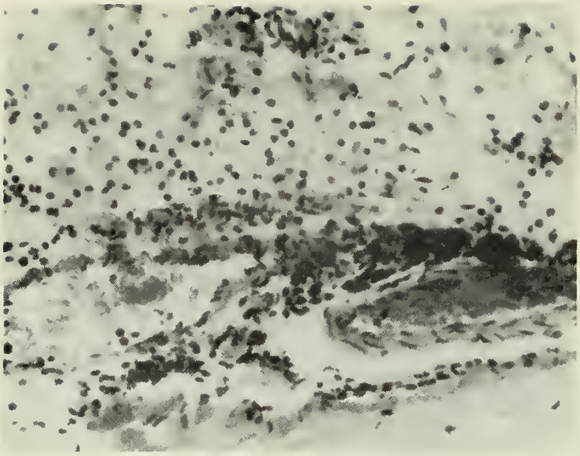


Fig. 6. Four-hour (active Arthus) reaction from a guinea pig given a single 30-μg. protein N immunizing dose of alum-precipitated pyridine ragweed and an intradermal injection of 10 protein N of aqueous ragweed extract on day 82, showing thrombosis of one vessel, perivascular infiltration of polymorphonuclear leukocytes, and hemorrhage around the other vessel. Hematoxylin and eosin stain, × 100

demonstrate this, Dixon increased the rate of metabolism in rabbits by giving thyroid. When this rate was doubled, the half-life of gamma globulin decreased from 4.7 to 3.2 days, a significant decrease.

EXPERIMENTAL SERUM SICKNESS

Experimental serum sickness is a good laboratory model in which to study a variety of human diseases. In this experimental model, three different types of tissue reactions are produced. They resemble the tissue reactions of the hypersensitive states in man, namely, the immediate wheal and flare reaction, the local or Arthus phenomenon which occurs at two to six hours, and the delayed reactions which may start at six to eight hours, reaching their peak usually at twenty-four hours and sometimes at forty-eight hours.

The Arthus reaction is a local inflammatory reaction to the intracutaneous injection of specific antigen in a previously immunized rabbit or guinea pig that occurs in the skin within two to six hours after the injection. It is characterized by redness, central blanching at four to six hours in some, and induration of the skin. Microscopically, there is localized vessel thrombosis, marked infiltration of polymorphonuclear neutrophilic leukocytes, swelling of vascular endothelium, clumps of leukocytes and platelets with the clumps sticking to the vascular endothelium, and tissue necrosis, especially of arterial walls. The reaction gradually declines or may persist but will be less intense for twenty-four to forty-eight hours. This reaction requires circulating precipitating antibody and the interaction of antibody and antigen and probably takes place in the walls of the small blood vessels. Antibody does not have to be fixed to tissue, but complement appears to be needed to cause tissue damage with the complex.[20] This reaction, or one that resembles it, occurs in man after reinjection of foreign serum or other foreign substances (Fig. 6).

The delayed reaction is caused by something, possibly antibodies, intimately associated with lymphoid cells or their cell fragments, and it is sometimes referred to as a cellular antibody. Crowle, in a recent publication,[21] has called these cells antibody-carrying lymphoid cells, because the delayed hypersensitivity cannot be transferred to another animal unless the lymphoid cell or its fragments are transferred. Pappenheimer[22] has called it "transfer factor," implying a difference from antibody. It differs from antibody in that no gamma globulin is involved. Guinea pigs immunized with 10 μg. bacillus

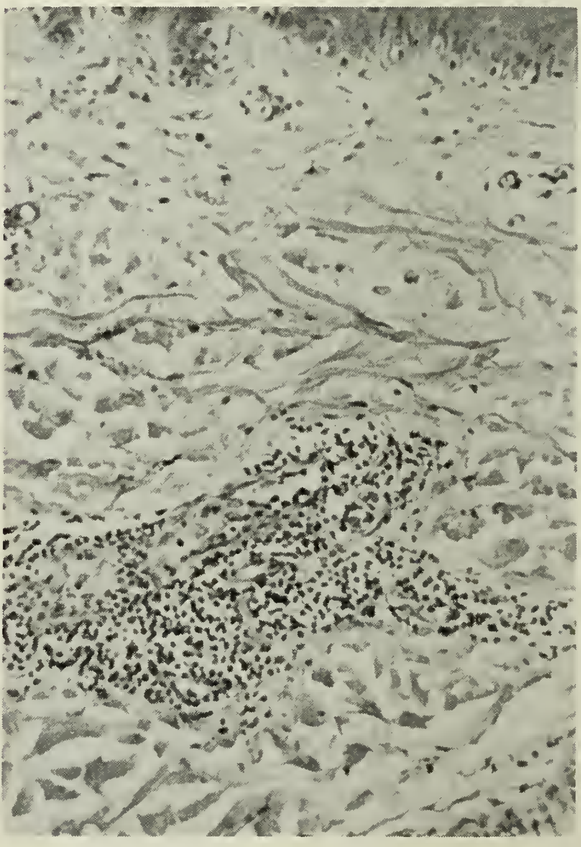


Fig. 7. Tuberculin skin test in a tuberculous guinea pig, biopsied at twenty-four hours, showing extensive perivascular infiltraton of essentially mononuclear cells in the dermis, with no vessel damage and no hemorrhage. Hematoxylin and eosin stain, × 60

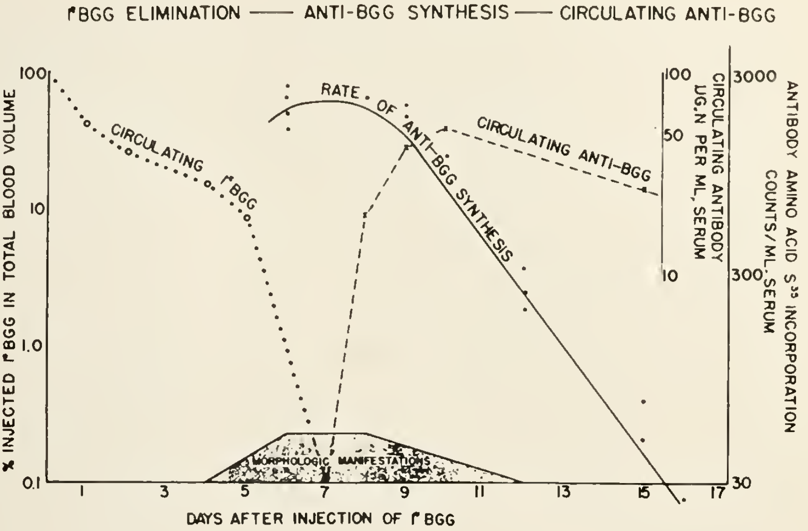


Fig. 8. Immunologic and morphologic events after the primary injection of I*BGG into rabbits[23]

Calmette-Guerin (BCG) organisms and seven days later skin tested with 1:50 dilution of old tuberculin had mild erythema and induration in six hours and marked erythema in twenty-four hours. Microscopically, these skin reactions showed moderate infiltration of cells, largely mononuclear, in the loose connective tissue between the corium and the muscular layer, as well as proliferation of mononuclear elements around arterioles, veins, and so forth. Polymorphonuclear eosinophils and neutrophils numbered less than one-third the total infiltrate at six hours. The vessels were dilated and there was mild edema. At forty-eight hours, almost all the cell infiltrate was mononuclear (Fig. 7).

The pathological changes in serum sickness, produced during the interval of five to twelve days after the injection, when antigen levels are low and the circulating antibody levels high, are proliferative glomerulonephritis, arteritis, and endocarditis, including valvulitis. The disappearance of serum sickness closely parallels the rise and fall of antibody synthesis. It is probable the antibody-antigen complexes that can be demonstrated in the circulation are caught in the walls of the glomerular capillaries and in other vessels to create these changes. The sequence of events in the immune response in serum sickness is shown in Figures 8 and 9.

In the experiment demonstrated in Figure 8, I*BGG is injected intravenously. The anti-BGG that is formed reacts with an excess of circulating antigen forming antibody-antigen complexes. The complexes circulate and are caught in certain tissues where chemical mediators are released that cause the inflammatory damage. By

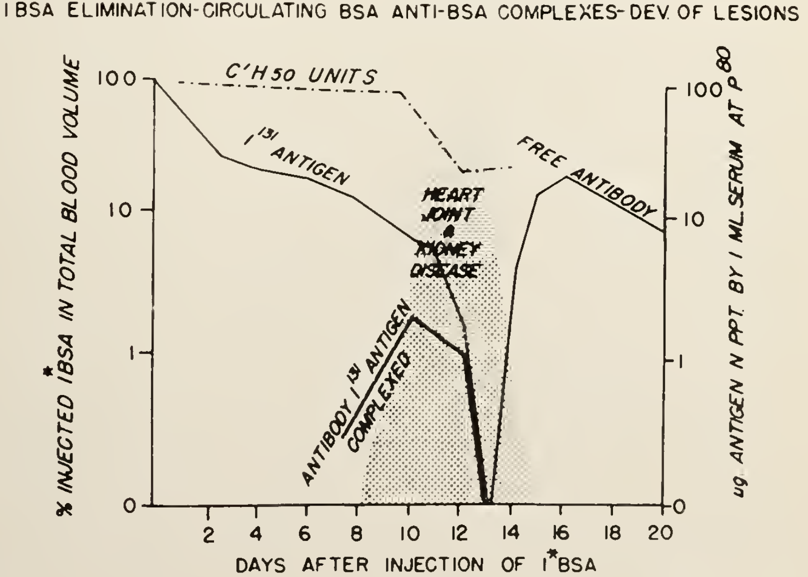


Fig. 9. Immunologic and morphologic events after the primary injection of I*BSA into rabbits[21]

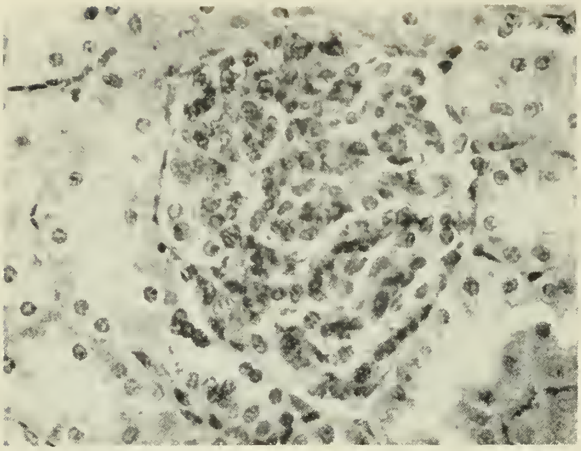


Fig. 10. Hematoxylin- and eosin-stained paraffin section of glomerulus of rabbit given injection of I*BSA two weeks previously. Typical proliferation of the epithelial and endothelial cells is evident. Tubules appear essentially normal.[23]

nine days, almost no antigen is left in the circulation; the dotted line shows this. The rapid elimination of the antigen takes place when there is a rapid formation of anti-BGG synthesis. The maximum concentration of free circulating anti-BGG is found about three days after complete elimination of I*BGG. The period of development of morphologic manifestations of serum sickness is indicated by the shaded area.[23] These lesions appear while antigen is being rapidly eliminated, and they gradually disappear after the appearance of circulating antibody.

Figure 9 shows the percent of animals that developed the lesions just discussed and the time interval between the injection of I*BSA and the appearance of the lesions. It shows the appearance of the pathological lesions in the period when the antigen-antibody complex concentration is the greatest, namely, seven to fifteen days after injection. Simultaneously with the appearance of detectable antigen-antibody complexes in the circulation, there is a drop in complement to less than half the normal value.[24]

Figure 10 shows the glomerulonephritis that develops in rabbits with experimental serum sickness as a result of the antibody-antigen complexes caught in the kidney tissue. There is the typical proliferation of epithelial and endothelial cells in the glomeruli.[23] The tubules appear essentially normal.

The upper half of Figure 11 shows the electron microscopic picture of a normal rabbit glomerulus.[24] The capillaries are widely patent. The basement membrane is uniform, with a central dark and peripheral lighter zone. The epithelial cells are attached to the outer aspect of the basement membrane by regular thin foot processes. The lower half of Figure 11 shows the electron microscopic picture of the kidney of a rabbit with serum sickness. There is a disappearance of the foot processes normally seen in the basement membrane and a flattening of this membrane. This same tissue, removed from an animal during serum sickness and stained with the Coons' method of fluorescent staining for rabbit gamma globulin and rabbit serum albumin, shows both proteins and complement-rich deposits present in much greater amounts than in normal kidney glomeruli,[24] indicating that antigen-antibody complexes are contained in the inflammatory lesions of serum sickness. The

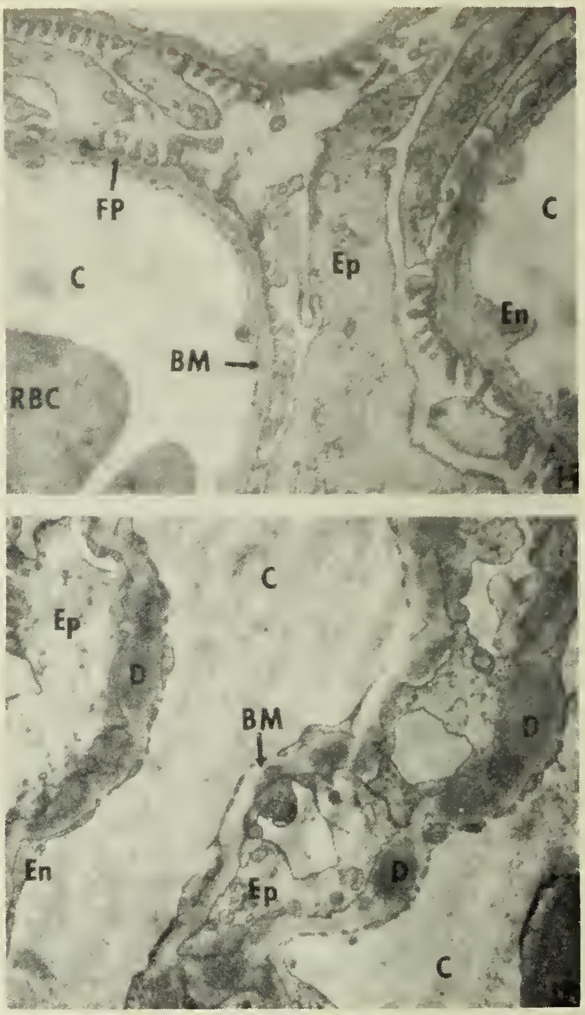


Fig. 11. [Top] Normal rabbit glomerulus. [Bottom] Kidney from rabbit with experimentally produced serum sickness. There is a disappearance of the epithelial foot processes and a flattening and irregular thickening of the basement membrane. There are lumpy, dense deposits along the outer aspect of the basement membrane.[24] (C=capillaries, RBC=red blood cells, En=endothelial cell, BM=basement membrane, Ep=epithelial cell, FP=thin foot process, D=deposits)

greatest tissue damage occurs when the antibody-antigen complexes are found in the presence of moderate antigen excess.

SERUM SICKNESS IN MAN

The development of serum sickness in man depends upon several factors. Heredity is probably not one of them. The dose of the serum that the patient gets is an important determining factor. The antigen involved in serum sickness may be the classical one, horse serum, or it may be a purified serum component such as bovine serum albumin. Other antigenic substances—for example, penicillin, bacteria, or metabolic products—may be involved. The interesting immunologic characteristic of this illness is that it illustrates one or all of the three different tissue reactions due to different types of antibody.

Types of antibody. [1] The precipitating antibody can cause the immediate local reaction around the injection site, as well as systemic anaphylaxis. Antibodies are circulating when the shot is given. [2] The nonprecipitating antibody, both skin-sensitizing (reagin) and non-skin-sensitizing (blocking), can exist in serum sickness with urticaria and angioedema. [3] One of the most universal types of reactions is due to the delayed hypersensitivity. Ninety-nine to 100% of the population have the capacity to develop this. This is the reaction that develops a few hours, six or so, to twenty-four hours after the injection is given. This type of reaction has already been described and is best exemplified by the various degrees of reaction that occur in the tuberculin test. It is often used synonymously with, and referred to as, tuberculin hypersensitivity. There is a predominance of lymphocytes microscopically in these lesions. These patients do not get immediate anaphylaxis, but they may go into delayed shock. As has already been said, one or all three of these tissue reactions can occur in serum sickness.

Frequency of serum sickness in relation to dose of antigen. Eighty-five percent of human beings would get serum sickness with a 100- to 200-ml. dose of sera, whereas only 20% would do so with a small dose of 2 ml. if whole horse serum was used. However, fractionated horse serum is now being used, and the number of cases of horse serum sickness has decreased. This means less antigen, especially in the material itself, and less total quantity getting into the host. This eliminates the albumin fraction of the serum which is more antigenic than the globulin fraction.

Reinjection. On reinjection, 90% of human beings would get serum sickness. On reinjection when antibody is present in the body, there is an immediate local reaction at the site of the injection, and the best example of this is the large, tender, painful, inflammatory mass that may develop at the point of injection after penicillin. The local reaction is similar to that described as the Arthus reaction in immunized rabbits or guinea pigs. The reaction is mediated by precipitating circulating antibodies, and the antibody-antigen complexes are acting at the local level.

It is also possible to get an immediate general reaction (anaphylaxis). For example, with bee or wasp stings or penicillin, even death may occur.

Latent antibody. When the antibody mechanism is latent, even after many years, an accelerated type of reaction can occur from a drug. There is no local reaction, but several hours or five to seven days after the drug is given, a less severe reaction may show up in the form of an erythematous rash. This reaction presupposes absence of circulating antibody in the body. It is referred to as latent because some antibody may be lurking around either in or on body cells of the host.

The clinical picture of serum sickness in man is beautifully summarized and the signs and symptoms synchronized in Figure 12, which was

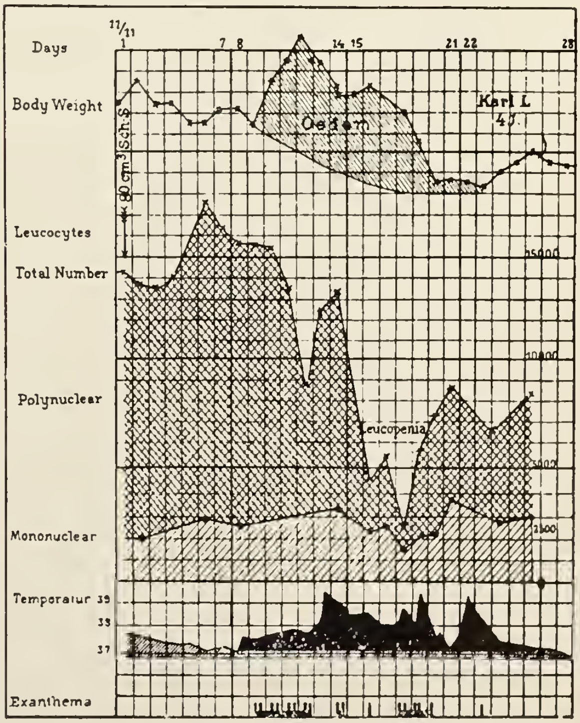


Fig. 12. The symptoms and signs of horse serum sickness, synchronized to show the fluctuations in body weight due to edema, leukocyte count, temperature, and rash related to day of injection of serum[23]

taken from the original description of serum sickness by Von Pirquet and Schick, written in 1905.[25] The typical serum sickness originally described was due to horse serum. The pathogenesis and immunology of serum sickness in man appear to be identical with those in experimental animals just described.

Clinical picture of serum sickness. The clinical signs of this condition usually develop eight to twelve days after the dose of offending antigen is received. The prodromal symptoms include inflammation at the site of the injection and slight swelling of the regional lymph nodes. There is usually fever. The skin eruptions may be urticaria, diffuse erythema, a morbilliform eruption, or an exudative, polymorphic type of eruption. At the height of the illness there is usually a sudden fall of polymorphonuclear cells. There is usually a generalized lymphadenopathy. Edema of subcutaneous tissues, especially of the face, hands, and feet, is common. Joint pains occur in about 2% of the patients. Abdominal pain and peripheral neuropathy can occur. A urinalysis occasionally shows albumin, hyaline casts, and erythrocytes.

Treatment of serum sickness. The treatment of serum sickness is always supportive and includes rest, cool compresses, and analgesics for comfort. Antihistamines may be given for relief of itching and to obtain rest. The use of steroids is very important unless the symptoms are very mild; without steroids, the symptoms may persist for three to four weeks. Steroids are thought to have an anti-inflammatory action, and they probably increase the histaminase activity. They decrease the formation or release of the chemical mediator, histamine, into the tissues. Perhaps steroids are responsible for specific interference with the antigen-antibody reaction that results in the release of the histamine.[2]

Prevention of serum sickness. Prevention of serum sickness is best accomplished by promoting widespread use of active immunization, even in adults. One should be aware of and remember that potent allergens can be found in many immunization products pediatricians use, such as pertussis products (rabbit serum), rabies vaccine (brain tissue), duck egg rabies vaccine (egg protein), and poliomyelitis vaccine (faint traces of horse serum, 1:5,000,000 monkey kidney protein, and, in most preparations, penicillin). Snake and black widow spider antiserum contains horse serum. This does not preclude using these products when really needed.

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Thrombocytopenia in Premature Infants

A. GÜLEN ÖZTALAY, M.D., ALICE GAMBLE BEARD, M.D.,
and F. STANLEY PORTER, M.D.

Little Rock, Arkansas

IN THE PAST, thrombocytopenia has been considered a rare finding in newborn infants and, when found, has usually been linked with neonatal sepsis,[1] transplacentally acquired infection such as rubella,[2] or maternal thrombocytopenia.[3] Recently Kaplan and Klein[4] reported a syndrome characterized by thrombocytopenia and mild intestinal bleeding without diarrhea occurring as a continuing outbreak. Thrombocytopenia was found in 21% of this large series of serially studied premature infants. The present study compares the incidence of thrombocytopenia associated with diarrhea with the incidence of thrombocytopenia in the general premature population and studies the number and morphology of megakaryocytes in infants with thrombocytopenia.

MATERIAL AND METHODS

To evaluate the frequency of thrombocytopenia in diarrhea as well as in the general premature population, a platelet count was obtained during the first two weeks of life on 93 of 107 premature infants admitted into the premature nursery of the Arkansas Medical Center during the first six months of 1963. The 14 infants not studied either died in the immediate neonatal period or were over two weeks of age when admitted. Twenty-four tibial bone marrow aspirations were obtained from 19 premature infants within twenty-four hours of the recognition of thrombocytopenia.

Platelets were enumerated by standard hematologic techniques.[5] All platelet counts under 100,000 per cubic millimeter were considered decreased[6] and were repeated weekly until normal. Weekly hemoglobin and reticulocyte counts were obtained in all infants, while capillary bleeding times[7] and tourniquet tests[8] were done only on thrombocytopenic infants.

After delivery all premature infants were placed in an Isolette with a temperature of 88 to 90° F. and 60% humidity. They were given 1 mg. of menadione sodium bisulfite intramuscularly on admission and were usually fed within the first twenty-four hours. Vitamin ACD, 0.3 ml., and ferrous sulfate (Fer-in-sol®), 0.3 ml., were given daily by mouth after the first week.

RESULTS

The distribution of thrombocytopenia among the 93 serially studied premature infants is depicted in Table 1. Eleven infants had diarrhea during the six-month period and, of these, 7 had neither thrombocytopenia nor bloody stools during the illness. Of the 4 infants with diarrhea and thrombocytopenia, 2 had fresh blood streaks in the stools (Cases 2 and 3, Table 2). Although pathogens were obtained from the nares and urine (Cases 3 and 4, Table 2), organisms other than nonpathogenic Escherichia coli were not cultured from the stools of any of the 11 infants.

TABLE 1

INCIDENCE OF THROMBOCYTOPENIA AMONG 93 SEQUENTIALLY STUDIED PREMATURE INFANTS HAVING INITIAL PLATELET COUNTS IN THE FIRST TWO WEEKS OF LIFE

I. Diarrhea		11
Thrombocytopenic	4 (36%)	
Nonthrombocytopenic	7 (64%)	
II. "Well" premature infants		
Thrombocytopenic	11 (14%)	
Nonthrombocytopenic	65 (86%)	
III. Infection (sepsis, pneumonitis)		2
Thrombocytopenic (sepsis)	1	
Nonthrombocytopenic	1	
IV. Postexchange		4
Thrombocytopenic (with sepsis, 2)	3	
Nonthrombocytopenic	1	
Total		93

A. GÜLEN ÖZTALAY *was research fellow in pediatrics, 1962-1963,* ALICE GAMBLE BEARD *is associate professor of pediatrics, and* F. STANLEY PORTER *is associate professor of pediatrics, University of Arkansas Medical Center, Little Rock.*

Dr. Porter's present address is Department of Pediatrics, Duke University School of Medicine, Durham, N.C.

TABLE 2

PERTINENT CLINICAL DATA ON FOUR INFANTS WITH THROMBOCYTOPENIA AND DIARRHEA

Name, race, sex	*Birth date*	*Birth weight (gm.)*	*Age at onset of diarrhea*	*Duration of diarrhea*	*Pertinent findings*	*Cultures*	*Treatment*	*Platelets per cu. mm.*	*Duration of thrombo-cytopenia*	*Megakaryo-cytes*
Da C/f	12/29/63	1,430	4 days	10 days	Hyaline membrane disease at birth, dehydration	Blood, negative; nose, negative; stool, negative	Kanamycin sulfate	50,000-70,000	3 weeks	Adequate
Ha "A" C/m	2/28/63	1,340	7 days	1 day	Respiratory distress at birth, bloody stool, dehydration	Blood, negative; nose, negative	Neomycin	57,000-89,000	4 days	Adequate
Ha "B" C/f	2/28/63	1,176	7 days	13 days	Respiratory distress at birth, bloody stool, dehydration	Blood, negative; nose, E. coli; stool, negative	Neomycin, chloramphenicol (Chloromycetin®), steroids, blood	31,000-83,000	4 weeks	Absent
McDo C/m	4/ 3/63	1,300	20 days	7 days	Hyaline membrane disease—exchanged at 4 days, platelets = 90 cc.^{2}—3 days, post-exchange, normal, 11 days later	Blood, staph. aureus; nose, staph. aureus; urine, 10,000 E. coli/high power field	Kanamycin sulfate	59,000-83,000	10 days	Adequate

Thrombocytopenia was recognized in all before antibiotics were instituted. Platelet counts varied from 52,000 to 83,000 per cubic millimeter in the thrombocytopenic infants; from 139,000 to 344,000 per cubic millimeter in the nonthrombocytopenic infants with diarrhea.

Eleven apparently well premature infants had platelet counts during the first two weeks of life which ranged from 50,000 to 90,000 per cubic millimeter while the remaining 65 well premature infants with platelet counts over 100,000 had an average platelet value of 200,800 per cubic millimeter (Table 1).

The maternal records on all thrombocytopenic infants were reviewed for evidence of administration of thiazide derivatives,[9] maternal infection such as rubella, and idiopathic thrombocytopenic purpura. One infant who at autopsy had intraventricular hemorrhage had a mother with idiopathic thrombocytopenic purpura.

The initial platelet counts were obtained during the first week of life in 62 infants. Distribution of these values by birth weights above or below 1,700 gm. are given in Table 3. Platelet counts for both sick and well infants under 1,700 gm. at birth were lower than in the larger infants. Thrombocytopenia occurred with illness more frequently in the lower weight group and was present in 7 of the 16 infants in this weight group. Repeat platelet counts after five to seven days on all infants whose initial platelet counts were under 100,000 per cubic millimeter, revealed normal values except for the 6 sick infants weighing less than 1,700 gm., whose values returned to normal in ten to twenty days.

In the 4 infants who had exchange transfusions for hyperbilirubinemia associated with Rh incompatibility, 2 had associated sepsis. Thrombocytopenia persisted for the first postexchange week, but platelet counts in all were normal twenty-one days after the procedure.

Hemoglobin values were above 13 gm. percent while reticulocyte counts were between 1 to 7% in all infants. Capillary bleeding and tourniquet tests on thrombocytopenic infants were normal.

Twenty-four bone marrow aspirations were done on 19 thrombocytopenic premature infants; 7 had diarrhea, 10 were apparently well, and 2 had had examinations following exchange transfusions. The bone marrow specimens obtained were uniformly dilute. However, if 2 or more megakaryocytes were seen on each of 4 coverslips examined, they were considered to be normal in number. If at least one-half of the megakaryocytes seen were producing identifiable platelets, they were considered to be normal in function. With these criteria in mind, all of the

TABLE 3

DISTRIBUTION OF PLATELET COUNTS DURING FIRST WEEK OF LIFE IN INFANTS GROUPED BY BIRTH WEIGHT

(The number of babies in each range is given in parentheses. Infants' initial counts during the second week are not included.)

	Weight (under 1,700 gm.)			*Weight (1,700-2,500 gm.)*		
	No.	*Average/cm.*	*Range*	*No.*	*Average*	*Range*
Well	8	158,000	80,000 (1)	41	177,000	42,000- 95,000 (4)
			114,000-258,000 (7)			106,000-213,000 (37)
Sick	8*	125,000	56,000- 93,000 (6)	5†	225,000	141,000-436,000 (5)
			108,000-294,000 (2)			
Total	16	144,000		46	182,000	

*Sick infants had: diarrhea (4), exchange transfusion (3), and sepsis (1).

†Sick infants had: diarrhea (3), pneumonitis (1), and exchange transfusion for isoimmunization (1).

bone marrow specimens examined exhibited normal numbers of platelet-producing megakaryocytes except for 1 infant (Case 3, Table 1) who had a normal platelet count during the first week of life. However, with the onset of diarrhea, both thrombocytopenia and the absence of megakaryocytes in the bone marrow were demonstrated; a finding which persisted for two weeks after the stools became normal.

DISCUSSION

In 1962, Kaplan and Klein[4] reported on 302 infants whose platelet counts were determined weekly; 64 (21%) had counts less than 100,000 per cubic millimeter and of these, 13 had intestinal bleeding. Bone marrow examinations were obtained on 3 of the 64 thrombocytopenic infants and were reported to be normal.

Since decreased numbers or absence of the megakaryocytes in the bone marrow are seen with both viral and bacterial infections and since about 40% of the cases of thrombocytopenia in the present series were associated with diarrhea, it seemed important to evaluate the appearance of the bone marrow during the period of thrombocytopenia. In none of the apparently well infants with thrombocytopenia and in only 1 of the 4 infants with diarrhea and thrombocytopenia, was there reduction or absence of megakaryocytes, suggesting that the thrombocytopenia is not frequently associated with inadequate platelet production.

Medoff[10] has recently reported the results of serial platelet counts in 26 premature infants and found them to range from 30,000 to 197,000 per cubic millimeter. Those under 1,700 gm. of body weight had lower platelet counts which persisted longer than those over this weight. Though the present study had few serial evaluations, slightly lower platelet counts were seen during the first week of life in infants under 1,700 gm., particularly when that infant was ill.

CONCLUSION AND SUMMARY

In the present series, thrombocytopenia was found in 21.5% of the 93 premature infants studied, occurring in about 14% of the apparently normal premature infants and lasting for less than two weeks. This thrombocytopenia may represent a more common finding among the premature population than originally realized. The incidence of thrombocytopenia associated with diarrheal infection was 36%, suggesting that illness and stress may increase the likelihood of thrombocytopenia.

Of 93 serially studied premature infants, 11 had diarrhea and, of these, 4 had thrombocytopenia. Thrombocytopenia was found in 21.5% of the 93 premature infants studied and occurred about 2.5 times more frequently in the group having diarrhea than in the normal premature infants.

Megakaryocytes were absent in only 1 of the 19 thrombocytopenic infants whose bone marrow was examined.

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The Importance of Atypical Mycobacterial Disease in Childhood

WILLIAM E. POTTS, M.D.

Little Rock, Arkansas

The fact that mycobacteria other than the human or bovine tubercle bacilli do cause significant amounts of disease in human beings has been well established by the evidence published in recent years. These organisms have been called anonymous mycobacteria, atypical mycobacteria, or unclassified mycobacteria. The consensus of opinion[1] now seems to be that the appropriate term should be atypical mycobacteria, as compared with Mycobacterium tuberculosis bovis, and for this reason they will be given this title throughout the paper.

Historically, the efforts to ascribe a place for these organisms among the list of microorganisms pathogenic for human disease date back many years. However, the first report, which included enough information to make this a well-established fact, was published by Timpe and Runyon[2] in 1954. Further categorization by bacteriological, chemical, and morphologic behavior and relationship to human disease is continuing, and some members of the various groups pathogenic for man have been accepted as distinct species of the genus Mycobacterium.

The majority of reports which describe disease caused by these microorganisms deal with disease of the lungs in adults, although occasional papers concerned with reports of disease in childhood have been published. In addition to disease states, delayed hypersensitivity of a tuberculin type to antigens prepared from these organisms is recognized, and appropriate skin test antigens are being produced and studied. The important fact that these organisms can produce nonspecific tuberculin hypersensitivity which can be elicited by testing patients with standard tuberculins has been well described by Edwards[3] and others. Standard commercial purified protein derivative (PPD) and U.S. Public Health Service (International Standard) PPD-S are made with a mixture of human and bovine strains.

Although clinical disease caused by the atypical mycobacteria is most often seen in adults, a review of the relationship of these organisms to disease in childhood is indicated. This discussion will concern itself with the nature of these organisms, clinical disease states in childhood caused by these organisms, and the influence these organisms may have on tuberculin testing. Although the source of infection with these organisms is generally unknown and man-to-man transmission has not been demonstrated, some consideration must be given to the possible epidemiology of these infections, including the reported geographic differences in their distribution.

THE NATURE OF THE ORGANISMS

The table describes the classification system most frequently used for reference and some of the characteristics of the various pathogenic atypical mycobacteria. The human and bovine tubercle bacilli are included for comparison. Although classification of the large group of atypical mycobacteria is not complete, the basic grouping described by Runyon has been recognized as a sound basis for further discussion and study.

CLINICAL DISEASE IN CHILDHOOD

Review of the literature immediately reveals two distinct situations in which infections in childhood caused by atypical mycobacteria are reported. The first of these situations is the reporting[7–9] of infection confirmed only by demonstration of delayed hypersensitivity to antigens prepared from the various groups of atypical mycobacteria. These reports include no pathologic material which will satisfy the criteria needed to establish a cause-and-effect relationship of organism to disease. The use of the term "presumptive" infection to describe these cases seems justified.

WILLIAM E. POTTS *is clinical assistant professor of pediatrics, University of Arkansas Medical Center, Little Rock.*

SOME CHARACTERISTICS OF PATHOGENIC MYCOBACTERIA[1-6]

Common name used to refer to organism	*Colonial morphology*	*Pigment production*	*Preferred temperature[1] growth rate on initial isolation*	*Catalase activity*	*Neutral red reaction*	*Niacin production*	*Human disease most frequently associated*	*Material for Mantoux skin test*	*Progressive disease in animals*
Human tubercle bacillus (M. tuberculosis)	Smooth or rough, eugonic to dysgonic, tight cording	None, appears slightly buff to brown in old colonies	Grows at average of 4 to 6 weeks at 37° C.	Moderate	Red	Only mycobacterium producing niacin	Pulmonary and so on	PPD-S, PPD commercial, OT commercial (and in some state laboratories)	Guinea pigs and mice; less frequent in rabbits
Bovine tubercle bacillus (M. bovis)	Similar to human strains	Same as human	Same as human	Moderate	Red	None	None recognized at present in United States		Kills rabbits and guinea pigs; disease in cattle is classic
Photochromogens, group I of Runyon (M. kansasii)	Smooth, occasionally rough, loose cording	None when in dark,[2] bright yellow to orange or brick-red in light	Grow slightly faster than human tubercle bacilli[3] at 37° C.	Usually vigorous	Brick dust	None	Pulmonary (scrofula reported Southwestern United States)	PPD-Y, photochromogen tuberculin[4]	Mice with exceedingly large inoculum; not guinea pigs
Scotochromogens, group II of Runyon	Smooth, eugonic or occasionally dysgonic or in thin film	Yellow or orange in light or dark	Grow slightly faster than human bacillus at 37° C.	Vigorous	Yellow to brick dust	None	Rarely pulmonary (scrofula reported in North Central United States)	PPD-G, PPD-216, scotochromogen tuberculin[4]	Mice with exceedingly large inoculum; not guinea pigs
Nonphotochromogens, group III of Runyon (Battey bacilli)	Small, smooth, circular, sometimes rough and dry	Weak or none, not related to light, darkest is buff to slightly yellow	Same as I and III, but grow at 45° C.[5]	Usually vigorous, some weak to moderate	Yellow	None	Pulmonary (scrofula rare)	PPD-B, PPD-240, PPD-269, PPD-63, nonchromogen tuberculin[4]	Not uniform; most will infect mice, not guinea pigs
Rapid growers, group IV of Runyon (M. fortuitum)	Fortuitum rough, others smooth	Some strains photochromogenic, fortuitum pigmented	Grow in 48 to 72 hours at 28 to 35° C., others grow at 30 to 45° C. in 3 to 4 days	Moderate to vigorous	Yellow	None	Pulmonary, disseminated	PPD-F (from fortuitum strain)	Not pathogenic for rabbits or guinea pigs; kills mice
M. balnei (M. marinum[6])	Smooth, rarely rough	Yellow in light	Grows in 1 to 2 weeks at 30° C., not at 37 or 45° C.	Moderate	Yellow	None	Swimming pool granuloma	Prepared by Scaefer as tuberculin	Not in guinea pigs, rabbits, or mice; causes ulceration in mice and rats
M. ulcerans	Very small, thin or droplike	None to very slightly yellow	Grows very slowly, up to 8 weeks at 30° C., none at 37° C.	Vigorous	Brick to red	None	Skin ulcer		Not in guinea pigs, rabbits, or mice; mice and hamsters develop ulcerations on inoculation

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[1] On standard tuberculosis media; subculture frequently changes this by increasing growth rate and temperature tolerance.

[2] Small amount of light initiates pigment production; older colonies with increased light exposure reach darkest pigmentation.

[3] At 20 to 25° C., occasionally visible colonies appear as early as 3 to 4 weeks.

[4] Prepared by Chapman at Wm. Buchanan Laboratory, Dallas

[5] Some say those growing at 45° C. are avian.

[6] These have been reported as being identical.

The second situation in which studies of atypical mycobacterial infections in childhood are reported is the description of clinical disease from which an atypical mycobacterium was isolated upon culture of diseased tissue. These cases will be considered as "confirmed" cases.

Confirmed disease. The first confirmed case of atypical mycobacterial disease in childhood was reported by Beaven and Bayne-Jones[10,11] in 1930 and 1931. This organism was called the Ryan strain and was isolated from the pleural exudate of an 11-month-old child who had opacification of a hemithorax by X-ray. Extensive studies revealed this organism to be an acid-fast bacillus which grew so rapidly on initial isolation that it would today undoubtedly be classed as a group IV (rapid growers), with moderate pigment production. The chronic lung disease evidenced by this child was undoubtedly related to this organism. The child slowly recovered from the infection after about one year's illness. Although this is the first report of lung disease caused by atypical mycobacteria, it remains as one of the best studied cases reported in the literature.

In 1949, Cuttino and McCabe[12] reported a new organism which caused granulomatous disease. They initially described this organism as a strain of Nocardia and defined it as Nocardia intracellularis. With further study, it was later decided that this was indeed a mycobacterium. Their patient was a 34-month-old white girl who presented with an abdominal mass. Biopsy of this mass revealed an acid-fast organism. Treatment with promine and penicillin was unsuccessful, and at death the mass was found to be a coalescence of abdominal lymph nodes in a granulomatous mass of huge proportions.

On microscopic examination, large numbers of acid-fast organisms were found in the macrophages of the tissue. In addition, Langhans-type giant cells were present and contained acid-fast staining organisms. Lungs, liver, spleen, and bone marrow were invaded by the organisms, suggesting an acute or chronic septicemic phase during the illness.

The organism produced a yellow-to-orange pigment with age but was isolated within twenty-four to forty-eight hours on initial inoculation, suggesting a rapid-growing organism which would be placed in Runyon's group IV at the present time.

MacCallum first reported[13] in 1948 a new type of skin lesion in man from which an acid-fast bacillus was isolated. The organism has been characterized by various workers and designated as Mycobarcterium ulcerans. The disease associated with this organism is characterized by the indolent spread of an ulcerating lesion from an area of preceding induration. In this infection, the site of the initial lesion is frequently the site of a preceding injury of a minor nature. Most subsequent reports of this disease have been from Africa; however, further cases from Australia and some from North America are reported.

Very soon after the report of MacCallum, Lindell and Norden,[14] in 1950, reported granulomatous lesions of the skin in a large group of people. All of these people had used one swimming pool in the town of Örebro, Sweden. The lesions were seen most frequently around the elbows but were also seen on other parts of the body.

An acid-fast bacillus was isolated from the swimming pool these people had used and was seen on tissue sections taken from the lesions. This mycobacterium has been classified as Mycobacterium balnei. Recent outbreaks of this disease have been studied in Colorado, Hawaii, and in the Pacific Northwest. This organism can be distinguished from Mycobacterium ulcerans, and the nature of the disease is reported to be much less serious than disease produced by Mycobacterium ulcerans. Recently, the organism was found in the tropical fish aquarium of two patients suffering from similar lesions.[15]

Chronologically, the next report of a case of atypical mycobacterial disease in childhood was by Pollack and Buhler in 1951.[16] This patient was later reported,[17] in 1956, as one of a series of cases of disease due to atypical, yellow-pigmented mycobacteria. The patient was a 4-week-old premature infant, product of a seven-month gestation, who died at 6 weeks of age of progressive lung disease produced by an organism identified in tissue section as an acid-fast bacillus. In addition to diffuse bronchopneumonic consolidation, a hilar lymph node involved by the acid-fast organism responsible for the bronchopneumonia was noted. Liver and spleen contained miliary nodules with acid-fast organisms, suggesting a septicemic phase of the illness. The organism was not cultured from this infant, but the mother died of disseminated disease produced by an acid-fast, pigmented mycobacterium, which definitely was not a human-type tubercle bacillus. Runyon later classified this as a photochromogen (group I). The case report suggests that this infection may have been acquired prenatally or at birth.

In 1956, Prissick and Masson[18] reported cases of scrofula in children caused by chromogenic mycobacteria. Since that time, many other authors have reported this condition. The appearance of most cases is indistinguishable from scrofula caused by human tubercle bacilli. Etiologic diagnosis of any scrofulous disease now depends on identification of the specific organism, since organisms from all of the major groups of atypical mycobacteria have been found to cause this condition. Excellent reviews of a scrofulous disease and suggested treatment are more recently available.[19–23]

In 1958, van der Hoeven and assocates[24] reported the history of a 16-month-old Negro male who died from a disseminated mycobacterial disease with multiple areas of osteomyelitis, granulomatous lung disease, and widespread reticuloendothelial tissue involvement by the acid-fast organism. The organism produced no pigment and was slow-growing. It had characteristics very similar to avian tubercle bacilli but was not classed as such, since it was nonfatal when injected in a chicken. It can now be classed as a group III (nonphotochromogens) mycobacteria, many of which behave quite like the avian tubercle bacillus.

In 1960, Yakovac[25] reported the history of a 19-month-old Negro male who died from the effects of disseminated osteomyelitis due to a group III mycobacterium. While this case was associated with miliary disease of the liver, the major portion of the disease was in the bony skeleton, and a striking similarity to Letterer-Siwe's disease was reported. It may well be that this was a patient who initially had Letterer-Siwe's disease and who later developed an infection from an atypical mycobacterium (group III) in the previously affected areas.

In 1961, Bialkin and associates[26] reported two patients with disease thought to be caused by atypical mycobacteria. Their patients were 4-year-old and 10-year-old Puerto Rican girls. The disease was similar to primary tuberculosis or, perhaps more closely, to chronic pneumonitis. Although photochromogenic (group I) acid-fast bacilli were recovered in gastric washings in both cases, the disease was described only on X-ray, and these cases were not proved by pathologic studies, since the illness produced was mild and both patients recovered. More recently, the recovery of atypical mycobacteria from persons free from clinical disease has been reported,[27] and this suggests that these cases may have had positive sputum or gastric cultures without the organism which was recovered having been the causative agent of the disease.

In 1963 and 1964, Merckx and associates[28] reported one case of an 8-year-old female child who had group I organisms cultured from a lung lesion which was not classically granulomatous but was more suggestive of localized fibrosis and hemochromatosis. No further details of this child's illness were reported.

Additional cases of osteomyelitis and disseminated disease produced by atypical mycobacteria were reported by Krieger and associates in 1964.[29] The report describes two children who had scotochromogenic (group II) mycobacteria cultured from osteomyelitic lesions of long bone, membranous bone, and short bones of the hand. Both children also had chronic pulmonary disease, but this could not be definitely ascribed to the same agent.

EFFECTS ON TUBERCULIN TESTING

Considerable doubt as to the specificity of tuberculin testing has been raised in recent years. The most detailed work on this subject has been carried on by Edwards and Palmer, who in several articles[3,30,31] have detailed the nature of nonspecific tuberculin hypersensitivity. They have shown that reactions to human tuberculin which are of small magnitude may indeed be produced by hypersensitivity to mycobacteria other than human tubercle bacilli.

In addition, the work of Kniker[32] and others has plainly shown the multiplicity of antigens to be found in any strain of mycobacteria and has shown that many of these antigenic substances are shared by strains other than the human tubercle bacillus.

It appears that three phenomena of tuberculin testing may be related to atypical mycobacterial hypersensitivity: [1] "reversion" of positive tests to negative (loss of previously demonstrated hypersensitivity), [2] inexplicable tuberculin hypersensitivity in children who cannot be shown to have been in contact with cases of tuberculosis, and [3] abnormally high reactor rates in screening programs using Vollmer patch tests, tuberculin Tine tests, or Heaf (Sterngun) tests. The first two situations are closely related and can be examined together.

The loss of tuberculin hypersensitivity, which has been well documented by various authors, has been shown by two studies to be related to nonspecific tuberculin reactions. The first study, by Mellman,[33] showed 60% of a group of children losing tuberculin hypersensitivity; the second study, by Potts and Chapman,[34] showed a loss of tuberculin hypersensitivity in 70% of a group of children.

The first report revealed that only 17% of the

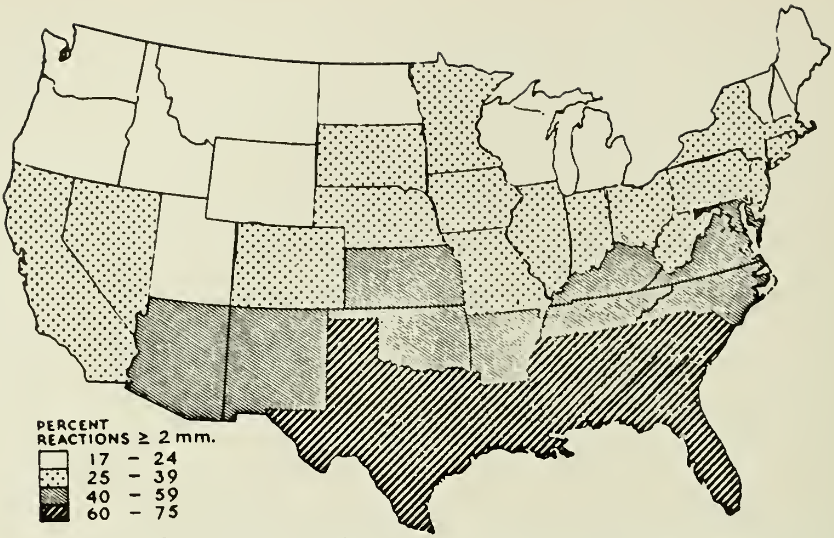

Fig. 1. Geographic variations in frequency of reactions to 0.0001 mg. of PPD-B among Navy recruits, indicating geographic distribution of hypersensitivity to Battey bacilli antigens[3]

group had been exposed to tuberculosis. In the second group, no contact with active tuberculosis could be found. In the second group, 66% of these children had been initially screened by the Vollmer patch test, leading to later Mantoux testing, which was initially positive. Repeated testing then demonstrated loss of hypersensitivity.

Both papers, as well as others considering the subject, show that the small-size initial reaction is characteristic for those who lose tuberculin hypersensitivity, but large-size reactors were included in the group, and both papers note a high degree of hypersensitivity to atypical mycobacterial antigens among those who reverted to negative.

The problem of the nonspecificity of positive reactions to Vollmer patch testing, tuberculin Tine testing, or Heaf (Sterngun) testing has been shown to be related to nonspecific hypersensitivity, apparently produced by atypical mycobacterial sensitization. Shaefer[35] noted high reactor rates to Vollmer patch tests among children who did not react to human tuberculin but whose specific sensitivity was to Mycobacterium balnei. Other atypical mycobacterial sensitization has also been shown to produce the false reaction with Vollmer patch testing. Hsu[36] has noted high rates of reaction to atypical mycobacterial antigens among children who were positive to Heaf testing but not to Mantoux testing. Hsu[36] also noted this to be true of testing with the tuberculin Tine test, showing that small-size Tine reactors frequently were PPD-S negative but positive to atypical mycobacterial antigens.

EPIDEMIOLOGY AND GEOGRAPHIC DISTRIBUTIONS

The epidemiology of atypical mycobacteria disease is poorly understood. The source of the infection has never been established, but reports of the occurrence of these organisms in the environment (with the exception of group I, photochromogens) are quite common. Studies[37,38] of household contacts have not established transmission from sputum-positive pulmonary cases to their contacts, nor has an epidemic of disease been recognized for the groups I through IV organisms. No vector or fomite has been discovered which can be related to clinical disease, and a reservoir in nature from which disease is transmitted has not been established.

It has been noted that one type of atypical mycobacteria produces a preponderance of cases of clinical disease in a geographic area and that the frequency of cutaneous hypersensitivity to PPD-atypical antigens is highest for the antigen homologous to the organism producing the greatest number of clinical cases in that area.

In addition, among childhood household contacts to adults with sputum-positive pulmonary disease, the incidence of hypersensitivity to a homologous antigen is greater than the incidence in the general population, although this incidence is only about half of that seen for positive tuberculin reactions among household contacts of patients infected with tubercle bacilli. This grouping of reactors about clinical cases does not, however, establish man-to-man transmission, nor has the reason for this grouping been elicited.

Geographic patterns of hypersensitivity are demonstrated in these figures from Edwards' work (Figs. 1 and 2).

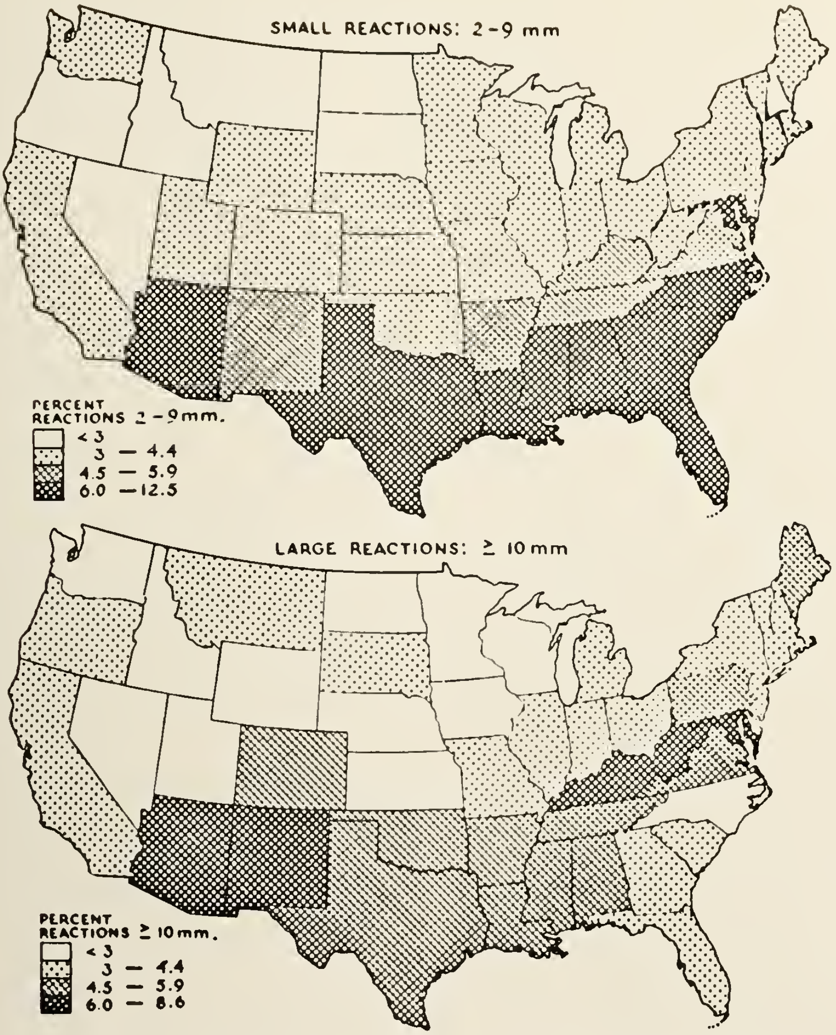

Fig. 2. Geographic variations in frequency of small and large reactions to 0.0001 mg. of PPD-S among Navy recruits, taken to indicate various atypical antigen hypersensitivity in small-size reactor figure, possibly group I hypersensitivity[3]

DISCUSSION

The similarities among different mycobacteria reported from human disease have led many people to conclude that all mycobacteria pathogenic for man are mutants of the Mycobacterium tuberculosis,[39,40] and it has been proposed that the cause of mutation is exposure to antituberculosis chemotherapy. It seems that this hypothesis is ill-founded on the basis of present information. The varying degree of pathogenicity, the selection of sites of disease in the body, and the wide variation in the intimate bacteriological characteristics of these organisms would be most easily understood by a taxonomist as indicating speciation rather than mutation. Runyon's statement[41] on the hypothesis that the atypical mycobacteria are mutants of human tubercle bacilli, arising from contact with chemotherapy, certainly seems to clearly and concisely refute such arguments.

It appears, then, that there are many mycobacterial species capable of producing disease, if the right circumstances are present, and that the human and bovine bacilli are only two species of a very large genus of mycobacteria. Just as diet, ethnic background, coexisting disease, and many other factors can be described which play an important role in the development of human tuberculosis, so it is possible to assume that the atypical mycobacteria are able to produce disease only when several factors in their favor are present. The nature of clinical disease produced by these organisms is certainly as widely varied as that produced by human tubercle bacilli. Reports not discussed are available describing more cases of each of the types listed in this paper.

As the awareness of these organisms as pathogens increases and as better identification of any

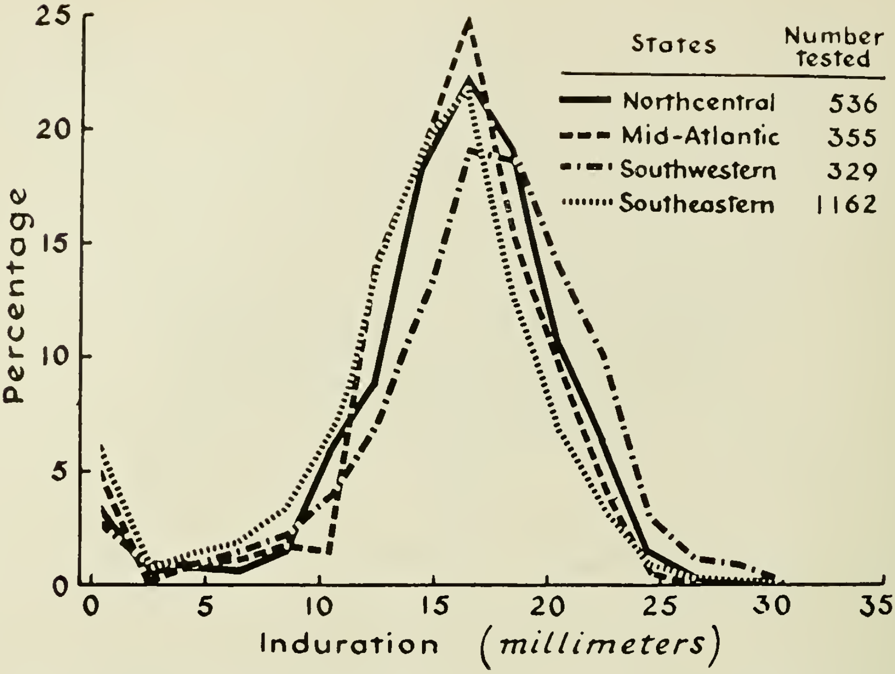

Fig. 3. Distributions of sizes of reactions to 0.0001 mg. of PPD-S among tuberculosis patients in four areas of the United States[3]

acid-fast organism by bacteriological laboratories is provided, more atypical mycobacterial disease will surely be reported. At present, the incidence of reactors to atypical mycobacterial antigens is much higher in some areas of the country than the incidence of reactions to human tuberculin, suggesting that more people have been infected with the atypical mycobacteria than with the human tubercle bacilli. This suggests frequent infection but also suggests a very low degree of pathogenicity for these organisms.

At present, the geographic incidence of homologous cutaneous hypersensitivity to atypical mycobacterial antigens parallels the case rate of clinical disease produced by these atypical mycobacteria. In addition, the rate of isolation of these organisms from the environment tends to parallel reactor rates. These facts suggest that the pathophysiology of disease produced by these organisms is similar to that of the human tubercle bacillus, with a childhood primary infection and endogenous reinfection disease in adult life. Proof for this hypothesis is lacking, since no report is available which clearly establishes that primary infections, similar to those of human tubercle bacilli, can be produced by atypical mycobacteria.

The geographic variation in distribution of human atypical mycobacterial disease and its close correlation to cutaneous hypersensitivity suggest that the source of the infection may vary from place to place; perhaps even multiple reservoirs are of importance in some areas. Certainly a knowledge of the geographic likelihood of encountering these organisms should improve the clinician's approach to this disease.

The solution of the immediate problem of production of antigens for skin testing, specific for each atypical mycobacterial type as well as the human tubercle bacillus, is a thing of the future. Until this problem is solved, the clinician is faced with the problem of distinguishing true positive tuberculin tests from nonspecific reactions (also called cross-reactions or false-positives). The best illustration of the nature of true tuberculin hypersensitivity is from Edwards' work[3] (Fig. 3), which shows the distribution of size of reaction to PPD-S among tuberculosis patients. One should notice that the distribution is nationally homogeneous. The small number of patients reacting below 10 mm. or above 25 mm. is also important. However, the overlap of this curve with curves from patients who give nonspecific reactions is considerable in some areas, and other information is needed to distinguish specific reactions. The use of contact evaluation to search for a source of infection and the use of repeated skin testing to show wide variations in degree of sensitivity sometimes help to clear up the confusion, since the specific reaction tends to be quite stable. With the present knowledge available about the atypical mycobacteria, the tuberculin skin test can no longer be considered as one of the more specific biological tests in man, and this knowledge highlights the importance of the use of other procedures before the diagnosis of tuberculosis is made.

At present, then, the frequency of disease caused by the atypical mycobacteria seems to warrant consideration of these organisms as the causative agent in several clinical situations, and each physician must, therefore, add the possibility of infection with atypical mycobacteria to his list of differential diagnoses when an appropriate situation is presented in clinical medicine.

SUMMARY

The atypical mycobacteria have now been recognized as a group of mycobacteria capable of producing human disease. Their nature and relationship to human and bovine tubercle bacilli are illustrated. A review of the various types of disease produced in childhood by these organisms is given, listing reports in chronological order. The problems that hypersensitivity to the atypical mycobacteria may produce when skin testing is done for tuberculin sensitivity are discussed. Some epidemiologic considerations are mentioned, and a description of the geographic distribution of hypersensitivity to the atypical mycobacteria is provided as an index of their distribution in the environment and in human disease.

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Erythrocyte Enzyme Deficiency Anemias in Children: A Review

D. H. BERRY, M.D.

Little Rock, Arkansas

THE ERYTHROCYTE ENZYME deficiency anemias are usually grouped as congenital nonspherocytic hemolytic anemias. Although this has long been recognized as a heterogeneous group, the anemias included have characteristics in common. They are hemolytic; the erythrocyte is nonspherocytic in shape and does not contain an abnormal hemoglobin and antibodies are not demonstrable by Coombs' tests. These anemias are congenital and often hereditary. They affect both sexes in all races and usually are not improved by splenectomy. The realization that this was a group of diseases led Selwyn and Dacie to further separate the group into type I and type II.[1] This separation is based on red cell morphology, the effect of incubation on osmotic fragility, the rate of spontaneous lysis of sterile incubated blood, and the effect of the addition of glucose on such incubation (see table).[2] De Gruchy and associates demonstrated that in type II anemias the increased autohemolysis is corrected by the addition of adenosine triphosphate (ATP).[3] The specific abnormality present in type II anemia was found to be pyruvate kinase deficiency.[4] Type I anemias still represent a heterogeneous group, although many in this group have been found to be due to a deficiency or abnormality of one or more enzymes used in glycolysis in the erythrocyte.

ERYTHROCYTE GLYCOLYSIS

The red cell needs no energy to perform its primary tasks of oxygen and carbon dioxide transport. However, energy is essential for the maintenance of the cell membrane, since the exchange of cholesterol and other labile stroma components is probably necessary for a viable cell. The property of semipermeability must be maintained. The passage of cations into the cell is against an ionic gradient which is known to involve ATP.[5] The net gain of two moles of ATP is achieved by anaerobic glycolysis in the erythrocyte. About 89% of the glucose metabolized by the red cell is through this cycle. This involves many enzymatically controlled alterations, in conjunction with coenzymes, to convert glucose to lactate (Fig. 1). The sequence of events falls into two functional halves. In the first functional half, glucose is degraded by a series of endergonic phosphorylactive processes to triosephosphate; in this process, ATP is consumed. Then the process is reversed, with a series of exergonic dephosphorylating reactions, with the formation of ATP. The rate-controlling steps are regarded as the hexokinase and the triosephosphate dehydrogenase reactions.

Much interest has been focused on the large amounts of 2, 3-diphosphoglycerate (2, 3-PGA) present in erythrocytes. With in vitro incubations using carbon 14–labeled glucose, as much as 90% of the glucose carbon has been found to pass through 2, 3-PGA.[6] The mechanism involved in synthesis and breakdown of this compound in vivo is uncertain. Rapoport and Luebering reported the presence of diphosphoglyceromutase which catalyzes 1, 3-diphosphoglycerate (1, 3-PGA) to 2, 3-PGA and of a phosphatase which catalyzes the conversion of 2, 3-PGA to 3-phosphoglycerate (3-PGA) and phosphate; 2, 3-PGA may be involved as a cofactor in the conversion of 3-PGA to 2-PGA. It has been proposed by Rapoport and Luebering that 2, 3-PGA represents a way of regulating the storage of energy in the cell, whereas hexokinase regulates the role of glucose utilization.[6]

About 11% of the glucose utilized by the erythrocyte is metabolized by the phosphogluconate oxidative pathway (Fig. 2). The prime importance of this pathway is in the production of reduced nicotinamide adenine dinucleotide phosphate ($NADPH_2$), formerly called reduced triphosphopyridine nucleotide (TPNH). This coenzyme is essential for the conversion of

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D. H. BERRY *is assistant professor, Department of Pediatrics, University of Arkansas Medical School, Little Rock.*

DIFFERENTIATION ACCORDING TO SELWYN AND DACIE[1] OF TYPE I and TYPE II NONSPHEROCYTIC HEMOLYTIC ANEMIA

	Type I	*Type II*
Red cells	Round, oval, or slightly ellipitic macrocytes	Round macrocytes
Osmotic fragility Fresh blood	Normal	Normal
Twenty-four hrs.' incubation	Slightly increased	Greatly increased
Autohemolysis (Forty-eight hrs. at 37° C.) Plain	Normal or slightly increased	Greatly increased
With glucose added	Diminished, but less than with normal cells	Not diminished

oxidized glutathione to reduced glutathione by glutathione reductase. In the red cell, the reduced glutathione functions to prevent the irreversible oxidation of hemoglobin. The coenzyme $NADPH_2$ also serves in the conversion of methemoglobin to oxyhemoglobin by methemoglobin reductase. Although methylene blue seems to stimulate the pathway, it is not the only one. Actually, the major pathway for conversion of methemoglobin by methemoglobin reductase utilizes reduced nicotinamide adenine dinucleotide ($NADH_2$),[7] formerly called reduced diphosphopyridine nucleotide (DPNH).

CLINICAL ENZYME STUDIES

For clinical significance, enzyme studies on erythrocytes must be related to both numbers and age of the erythrocytes. Misleadingly low enzyme levels have been reported when decreased red cell mass was not taken into account. The amount of some enzymes, the rate of glucose utilization, anaerobic glycolysis, and the exchange of cations are increased in the reticulocyte and young erythrocyte as compared to the aging cell.[5] Misleadingly high enzyme levels can be found during periods of brisk erythropoiesis.[8] Because of high enzyme content in leukocytes, contamination in some assays (particularly in pyruvate kinase) can be quite devastating.

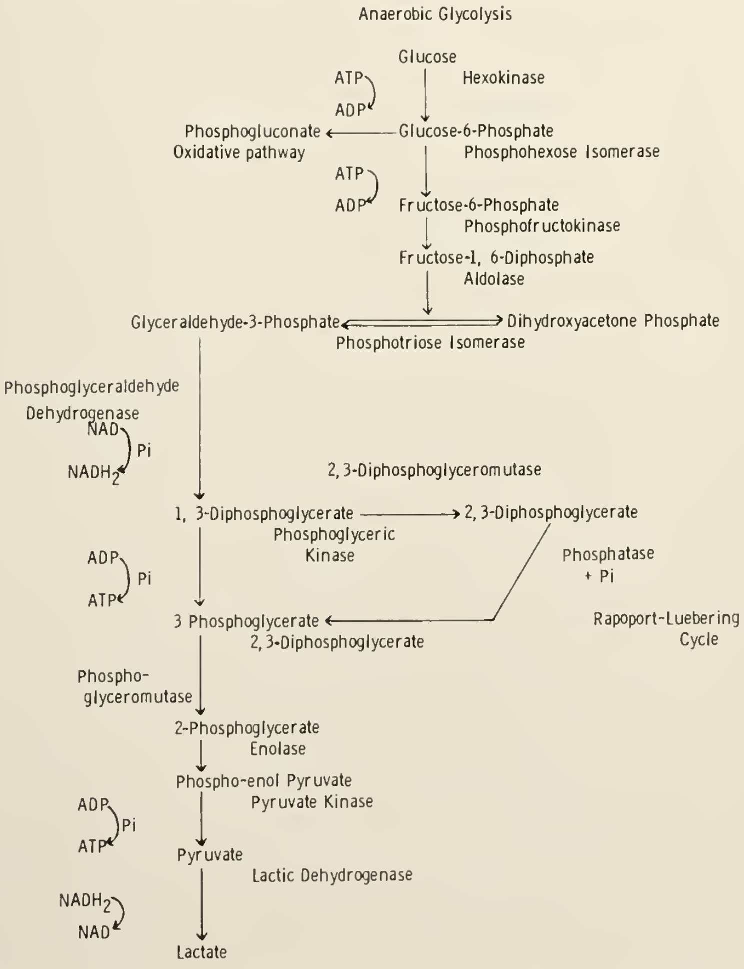

Fig. 1. Anaerobic glycolysis. This is the major pathway in the mature erythrocyte for glucose catabolism and energy production. (ATP, adenosine triphosphate; ADP, adenosine diphosphate; NAD, nicotinamide adenine dinucleotide; $NADH_2$, reduced nicotinamide adenine dinucleotide; Pi, inorganic phosphate)

Pyruvate kinase deficiency. In 1961, Valentine and associates reported the specific deficiency of pyruvate kinase (PK) in seven patients with characteristics of type II deficiency.[4] Subsequently, it has been emphasized that the block in glycolysis caused by the deficiency in PK prevents adequate ATP regeneration.[9] The clinical expression of this deficiency is variable, from requiring frequent replacement transfusions from birth to having the diagnosis made incidently during adulthood. This seems to be unrelated to severity of enzyme deficiency.[10] In general, the characteristics are those of a compensated hemolytic anemia. Although the degree of anemia and the elevation of the reticulocyte count are variable, both are constantly present. Splenomegaly occurs, but icterus and cholecystitis are inconstant features. In some patients, decrease in transfusion requirements occurs after splenectomy. The disease has been found equally in both sexes and only in Caucasians. Heterozygous and homozygous patients have been found in studies of families with the disease, indicating that this is a genetically determined disorder with an autosomal recessive mode of transmission. The erythrocytes are macrocytic and normochromic, with slight anisocytosis and poikilocytosis. The white cell and platelet counts are normal or reflect the effects of splenectomy.

Glucose-6-phosphate dehydrogenase deficiency. There are several hemolytic anemias with a basic deficiency of glucose-6-phosphate dehydrogenase (G6PD). Although these anemias share a similar defect in erythrocyte metabolism, the clinical manifestations are different. These include the primaquine-sensitive anemias found in Negroes, the G6PD deficiency in Caucasians, and the anemia secondary to the ingestion of fava beans in sensitive individuals (most commonly southern Europeans). In the latter, something in addition to decreased G6PD is thought to be present, because individuals with G6PD deficiency alone do not hemolyze after the ingestion of fava beans.[11]

G6PD deficiency in Negroes is inherited as a sex-linked gene of intermediate dominance. The incidence is 13% in males and 1 to 2% in females. The mutant X chromosome is unopposed by a normal allele in the hemozygous male.[12] Most females have partial expression of the trait, since the mutant gene must be inherited from both parents to have a homozygous female. The enzyme deficiency is limited to the erythrocyte and the lens of the eye. Alterations in the biochemical characteristics of the enzyme have been described but have not been directly related to the hemolytic process as found in Negroes.[13–17] These individuals have normal hemoglobin, normal reticulocyte count, and slightly decreased red cell survival. The occurrence of a hemolytic episode seems to be dependent on a combination of factors, such as exposure to the offending agent, other disease processes, and individual variation.[8] If these occur, the sensitive cells are rapidly destroyed because of irreversible denaturation of hemoglobin. Beutler demonstrated, by the use of iron 59–labeled erythrocytes, that the sensitivity to denaturation does not appear in cells younger than 63 to 75 days of age.[11] This occurs because G6PD decreases as the cell ages, until it reaches such a level that insufficient $NADPH_2$ is generated and, consequently, reduced glutathione is not available to protect the hemoglobin from denaturation.

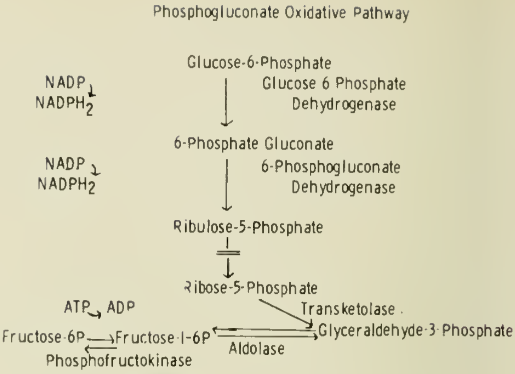

Fig. 2. Phosphogluconate oxidative pathway. Aerobic glycolysis in the mature erythrocyte provides reduced nicotinamide adenine dinucleotide, which is necessary for the reduction of glutathione. (ATP, adenosine triphosphate; ADP, pyruvate kinase; NADP, glucose-6-phosphate; $NADPH_2$, reduced nicotinamide adenine dinucleotide phosphate)

The offending drugs most frequently encountered in pediatric practice are vitamin K analogues, sulfonamides, chloramphenicol, and antipyretic agents. After initial hemolysis with continued administration of the drug, the sensitive individual develops a compensated hemolytic anemia. If the drug is discontinued and reinstituted at a later date when older erythrocytes are again present, quick hemolysis will ensue. If G6PD assay is performed on blood samples with elevated reticulocyte counts, misleadingly high values may be obtained.

The occurrence of G6PD deficiency in Caucasians is infrequent.[12] Although the mode of inheritance seems to be similar to that found in Negroes, the deficiency has been found to be present not just in erythrocytes but in leukocytes and platelets as well. Alterations in the biochemical characteristics have been described and several G6PD variants reported.[15–17] The individuals have decreased hemoglobins, constant reticulocytosis, and shortened red cell survivals. Macrocytosis with some anisocytosis has been described in peripheral blood smears of these individuals. Basophilic stippling has been observed. These patients seem to be exquisitely sensitive to hemolytic episodes when they are in the presence of offending agents or infections. The offending drugs are the same as in the Negro group, but the reactions to them are more severe in the Caucasian group.

Other reported erythrocyte enzyme deficiencies. In the last five years, several other erythrocyte enzyme deficiencies have been reported. Since these are mostly case reports, the complete biochmical characteristics and the clinical features of many of the deficiencies are uncertain.

Brewer and Dern have reported a Negro female with 6-phosphogluconate dehydrogenase deficiency.[18] In extensive studies of the kindred, the enzyme deficiency appears to be due to a simple autosomal dominant gene. Clinical features are not described.

Decreased glutathione reductase was reported by Carson in 1961.[19] Fornaini and associates described a family of three with glutathione instability but normal G6PD.[20] They found abnormalities in the glutathione reductase and methemoglobin reductase in these individuals. Two of the three cases reported had moderate anemia and intermittent icterus.

Bowdler and Prankerd[21] reported 2, 3-diphosphoglyceromutase deficiency. This was a male child who had intermittent attacks of abdominal pain, fever, and jaundice. The attacks subsided after splenectomy, but mild anemia, reticulocytosis, and icterus persisted. The boy's father was similarly affected.

Schneider and associates found triosephosphate isomerase deficiency in a female infant of French-Negro ancestry.[22] Family studies suggested an autosomal-recessive mode of inheritance. The infant had moderate anemia and reticulocytosis and had received several blood transfusions. Slight macrocytosis, small numbers of target cells, occasional nucleated erythrocytes, and polychromasia were noted on blood smear. Some densely contracted red cells with irregular margins were noted also.

Methemoglobinemia caused by a lack of $NADH_2$ diaphorase has been described.[23–25] Although there is no associated hemolytic anemia with this entity, it is included because it is due to an enzyme deficiency in the erythrocytes. Extensive family studies indicate that this is inherited as an autosomal recessive. The degree of cyanosis present is directly related to the amount of methemoglobin. The individual may be cyanotic constantly or only after exertion. Clubbing of digits is not present. The patient may exhibit dizziness, headaches, dyspnea on exertion, and general physical weakness. There may be a slight increase in red cell and white cell counts. The methemoglobin can be converted to oxyhemoglobin by the administration of methylene blue or ascorbic acid.

SUMMARY

Many hemolytic anemias due to erythrocyte enzyme deficiency have been delineated in the past decade. The most common erythrocyte enzyme deficiency anemias found today are those involving G6PD deficiency. Much interest has been generated in this area. With increased understanding of erythrocyte glycolysis, energy requirements, aging, and destruction, other entities should be defined.

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SYMPTOMS OF ACUTE LEUKEMIA, such as enlargement of peripheral lymph nodes and spontaneous bleeding, often appear at the beginning of the terminal phase of chronic myelogenous leukemia. Other symptoms in the one-to-three months before death are nonspecific and similar to those accompanying earlier exacerbations. Many of these patients may have an underlying acute disease. Acute leukemia appeared to supervene in 15 of 21 patients observed within fourteen days of death. Clinical and hematological changes were suggestive of acute disease in 3 and indeterminate in another 3.

GEORGE W. MORROW, JR., M.D., GERTRUDE L. PEASE, M.D., CHARLES F. STROEBEL, M.D., and WARREN A. BENNETT, M.D., Mayo Clinic and Foundation, Rochester, Minn. Terminal phase of chronic myelogenous leukemia. Cancer (Philad.) 18:369-374, 1965.

MULTIPLE BASAL CELL EPITHELIOMA may be associated with cystic lesions of the upper and lower jaw, varying from trichoepithelioma to ulcerative invasive growth. Common features of the syndrome—observed often in puberty—include bifid ribs, calcification of the dura or falx cerebri, broad nasal root, frontal bossing, scoliosis, and cutaneous pits on hands and feet. Usually located on the face, cysts often are asymptomatic but may impinge on developing teeth. Close watch for change in character is indicated and removal advised in the likelihood of fracture or if they appear to be ameloblastomas. Surgery is preferable to irradiation.

LYLE V. KRAGH, M.D., and JOHN K. GROTTING, M.D., Minneapolis. Multiple basal cell epithelioma; jaw cyst syndrome. Minn. Med. 48:575-576, 1965.

Late-Onset Branched-Chain Ketoaciduria (Maple Syrup Urine Disease)

M. D. MORRIS, Ph.D., D. A. FISHER, M.D.,
and R. FISER

Little Rock, Arkansas

BRANCHED-CHAIN KETOACIDURIA, otherwise known as maple syrup urine disease (MSUD), is usually manifest as a rapidly fatal disorder in which the clinical symptoms are accompanied by excretion of a characteristic pleasant-smelling urine.[1–4] A variant of the classical type has been reported in infants and children whose growth and development are not impaired and who, in addition, appear to be normal mentally.[5,6] These late-onset variants may show the first symptoms referable to branched-chain ketoaciduria as late as 8 years of age. In others, the first onset was at about 15 months. All of the late-onset patients, like those with the fulminating syndrome, show an elevated urinary excretion of leucine, isoleucine, and valine amino acids as well as the respective alpha-keto acids.

This paper deals with clinical and biochemical findings in still another patient with late-onset branched-chain ketoaciduria.

CASE REPORT

This Caucasian male was born September 9, 1959, the product of the fourth uneventful term pregnancy of a healthy 28-year-old Caucasian female. His postnatal course and early infancy were uneventful, and he was breast fed for approximately seven months. The last of his three siblings, a female born in 1957, had late-onset branched-chain ketoaciduria and was previously reported.[5] The remainder of the family history was negative. Because his sister had MSUD, urine examinations for abnormal amino acid excretion were conducted at 2 and 9 months of age and results were normal. At 10½ months of age, during the course of a mild respiratory infection, he became quite irritable and seemed ataxic while sitting. The diagnosis of MSUD was confirmed by the observation of increased excretion of amino and keto acids at that time. This episode was transient, lasting only forty-eight to seventy-two hours, and over the subsequent nine months symptomatology was minimal. Only occasional mild ataxia and questionably abnormal irritability were noted.

At 19 months of age, during a lengthy cross-country automobile ride, at which time his milk intake was increased, he became progressively irritable and ataxic. By the fifth day, he was semicomatose. He was hospitalized without oral feeding and responded within seventy-two hours to intravenous fluid therapy. Over a subsequent six-month period at home he remained quite irritable, cried frequently at night, could no longer stand or walk (he had walked alone at about 13 months), and had significant ataxia which was noted when he sat in a highchair. At 25 months of age he was taken off cow's milk which he had usually taken in amounts of 24 to 30 oz. daily. He then was restricted to a 12-oz. daily formula of Enfamil® and a low leucine diet consisting largely of fruits, vegetables, and cereals, with supplemental plain gelatin and multivitamins. On this regimen his symptoms again disappeared, and subsequent growth and development were normal.

He did not seem to be intellectually retarded compared with his two normal siblings or the neighborhood children. Objective testing was not performed, however.

During the fall and winter of 1963-64 he experienced several episodes of respiratory infection which, on two occasions, progressed to otitis media. Shortly after the second episode in February 1964, a tonsillectomy and an adenoidectomy were performed. Bleeding was noted a few hours postoperatively and he was returned to the operating room for suturing of the tonsillar fossa.

The bleeding recurred on the second hospital day. He was given a 500-ml. blood transfusion and was returned to the operating room for a third time for hemostasis. By the evening of the second hospital day he was semicomatose, with alternating periods of rigidity and flaccidity. There were no local or lateralizing signs; abdominal and cremasteric reflexes were absent. Fundi were normal and the cerebrospinal fluid pressure was 190 to 200 mm. of water. Therapy consisted of a laxative to rid the gut of unabsorbed blood, intravenous fluid therapy, hydrocortisone 21-sodium succinate (Solu-Cortef®), and an anabolic steroid. Over the subsequent five-day period there was progressive deterioration. Spontaneous respiration ceased on the fourth hospital day, and the patient was maintained subsequently with an endotracheal catheter, oxygen, and a Bennett respirator. His peripheral and corneal reflexes disappeared; his pupils became dilated and fixed. He died on the morning of the seventh hospital day.

Autopsy revealed a large amount of sweet-smelling peritoneal fluid and cerebral edema.

M. D. MORRIS *is associate professor of pediatrics and biochemistry,* D. A. FISHER *is associate professor of pediatrics, and* R. FISER *is a medical student, University of Arkansas Medical School, Little Rock.*

Fig. 1. The first three chromatograms show leucine, isoleucine, and valine amino acid spots from urine obtained on the second, third, and seventh hospital days. The fourth chromatogram shows valine and leucine standards.

METHODS

All urine specimens were placed in ice after voiding and were kept frozen at −20° C. until analyzed. Some of the samples were flown over dry ice from California to Little Rock.

Total direct keto acids were measured by the method of Friedemann and Haugen, using either alpha-ketoisocaproic acid or isovaleric acid as the standard.[7]

For identification of the individual keto acids, a sample of urine was allowed to react for thirty minutes at room temperature with 2, 4-dinitrophenylhydrazine. The keto acid hydrazones were then further purified by extraction with sodium carbonate. Following careful acidification of the sodium carbonate solution, the keto acid hydrazones were extracted with ether, dried over sodium sulfate, and hydrogenated in an alcoholic solution over platinum oxide. A standard keto acid was included in every run. The resulting amino acids were chromatographed in a water-solvent system of butanol and acetic acid, and they were visualized with ninhydrin.[8] Urine was chromatographed directly using the same solvent system, and the amino acids were visualized similarly.

RESULTS

Urine samples, obtained at 2 and 9 months of age were normal with respect to both qualitative and quantitative alpha-keto acids. At age 10½ months, the parents first noted ataxia and irritability accompained by the excretion of a pleasant-smelling urine. A urine specimen obtained at this time contained 1,080 μg. of alpha-keto acid per mg. of creatinine (normal for this age <100) comprised principally of leucine (isoleucine) and valine.

Figure 1 shows the results of urinary branched-chain amino acid chromatography on samples obtained from the patient during the second, third, and seventh hospital days following surgery. Volumes of urine representing approximately equal quantities of creatinine, which was used as an internal standard, were applied to each of these chromatograms. It is evident that, on a qualitative basis, more leucine, isoleucine, and valine were present in the second day's sample than in the others. At this concentration of creatinine, no leucine, isoleucine, or valine amino acids were observed in the urine sample obtained on the seventh hospital day.

Figure 2 shows chromatograms of the amino acids formed from the 2, 4-dinitrophenylhydrazines of the keto acids. Leucine was found in samples from the second and third hospital days but was not observed in the sample on the seventh day. Although not too evident from this photograph, valine also was found in the third day's sample. Only a trace of valine was observed in the seventh day's sample.

The table summarizes quantitative alpha-keto acid excretion on all urine samples studied.

DISCUSSION

By history and measurements of urinary amino and keto acids, the onset of clinical MSUD in this patient was delayed until 10½ months of age.

Fig. 2. The first three chromatograms show the amino acids formed from the 2, 4-dinitrophenylhydrazines of the keto acids of leucine and valine in the urine obtained on the second, third, and seventh hospital days. The fourth chromatogram shows the leucine standard.

Following this initial clinical episode, the patient had little or no difficulty until the age of 19 months. At this time a severe episode was followed by chronic symptoms which continued until he was placed on a diet restricting his intake of branched-chain amino acids. For the subsequent twenty-seven months, after the institution of this diet and before his demise, no major clinical exacerbations were noted.

During the fall and winter of 1963-64, when the patient had several bouts of intercurrent infection, no clinical exacerbations relative to branched-chain ketoaciduria nor any apparent odor were observed during this time. The patient fractured his left arm and right foot in 1963 and experienced no difficulty at that time.

The dietary history revealed a concerted effort to avoid milk and its products and to limit meat in the child's diet.

Patients with late-onset branched-chain ketoaciduria probably have a partial enzymatic defect in the metabolism of branched-chain keto acids which are derived from leucine, isoleucine, and valine by transamination. The metabolic aberration is especially apparent during stress. In the final hospitalization, the stress was complicated by blood loss into the intestinal tract and possible anoxia. The general catabolic state with its attendant blood loss undoubtedly provided an increased branched-chain amino acid load, which probably contributed in a major fashion to the clinical symptoms. The high values for urinary branched-chain keto acids and excessive branched-chain amino acids seen on the second and third hospital days are in accord with such a view. The reason for the low amino and keto acid levels in the urine obtained on the seventh hospital day is not apparent.

In spite of severe clinical involvement for short periods, patients with late-onset MSUD appear to have normal mental and physical development.[5,6] By contrast, patients with neonatal MSUD have severe and irreversible brain damage. This probably can be minimized by early dietary restriction of branched-chain amino acids.

Snyderman and co-workers[9] treated a patient with neonatal MSUD at 17 days of age with such a diet, but they reported moderate mental retardation at 54 months. Although treatment was complicated by periods of prolonged deprivation of methionine, these authors suggest that, among other things, the diet was instituted too late to prevent irreversible brain damage. Westall[10] treated an infant with neonatal MSUD from the age of 6 days with a diet containing

QUANTITATIVE URINARY ALPHA-KETO ACID EXCRETION

Date	*Alpha-keto acids mg. per gm. creatinine*
November 10, 1959	60
June 10, 1960	80
July 22, 1960	1,080
February 19, 1964	3,660
February 20, 1964	20,000
Controls	40 to 110

minimal amounts of leucine, isoleucine, and valine. At 1 year of age, the mental and neurological status of this child was normal. Thus, it would appear that the neonatal brain in the early-onset MSUD patients is particularly sensitive to high levels of branched-chain amino or keto acids. The reason for this sensitivity is obscure.

The authors are grateful to Dr. R. C. Conner of Oceanside, California, and Dr. R. E. Stang of Vista, California, for invaluable information and the provision of urine specimens during the most recent hospitalization.

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DEVIATION TO THE LEFT beyond −30° of the mean QRS axis in the frontal plane seldom occurs without associated left ventricular fibrosis or recent infarction. Myocardial fibrosis may exist, however, without left axis deviation. Significant left axis deviation may rarely be caused by: (1) various types of myocardiopathy, (2) congenital anomaly of the left ventricular conduction system, (3) atrial septal defect of the ostium primum or complete type, (4) ischemia, without fibrosis, of the left ventricular conduction system, and (5) pulmonary emphysema. Causes for left axis deviation under 30° include anatomic position of the heart, age, body weight, and left ventricular conduction disturbances.

ROBERT A. CORNE, M.D., THOMAS W. PARKIN, M.D., ROBERT O. BRANDENBURG, M.D., and ARNOLD L. BROWN, JR., M.D., Mayo Clinic and Foundation, Rochester, Minn. Significance of marked left axis deviation. Amer. J. Cardiol. 15:605-610, 1965.

MAMMOGRAPHY should be included in follow-up examinations after unilateral mastectomy for carcinoma to aid early detection of cancer in the remaining breast. Carcinomas are smaller and associated with fewer axillary lymph node metastases when detected by mammography than when found by palpation. Physical examination detected 15 tumors in the remaining breast in a study of 397 postmastectomy patients; 9 of the tumors were clinically malignant. Mammographic examination showed 6 tumors to be malignant and revealed unsuspected carcinoma in 10 other patients.

MICHAEL M. MISSAKIAN, M.D., DAVID M. WITTEN, M.D., and EDGAR G. HARRISON, JR., M.D., Mayo Clinic and Graduate School of Medicine, Rochester, Minn. Mammography after mastectomy. J. Amer. med. Ass. 191:1045-1048, 1965.

Lillian Mayer Fink. M.D.

L. F. RICHDORF, M.D.
Minneapolis

TO WRITE A BIOGRAPHY is a responsibility. One's first reaction is a feeling that occasions an exaggeration of that accountability. In general, it is well that the writer have had a long acquaintance with the person involved.

It comes as a surprise to me to reflect on the actual length of acquaintance with Dr. Lillian. It is, therefore, in the sense of friendship to a good neighbor that this is written.

It was in January of 1919 when I came to the University of Minnesota Medical School that I first met Lillian Mayer. We both graduated as M.D.s in the class of 1921. Close association in medical circles and hospitals since that time has familiarized me with some of Dr. Lillian Fink's interests. Our families have enjoyed many functions together, some medical in nature and others of recreation. Then too, there has been some exchanging of medical care.

Lillian Mayer was born in Great Falls, Mont., July 24, 1897, of John H. Mayer and Sophia Sosnick. The family had deep roots in Minnesota. The grandfather, John A. Mayer, was a friend of the famous James Hill, "Empire Builder" of railroads in the Great Northwest. The latter named the town of Mayer, Minn., in honor of his friend. The grandmother maintained her home in Delano, Minn., all her life, though she died in Great Falls. Lillian's father went to Great Falls to work as an office boy for his father in 1888, and the following year became a telegraph operator. In 1891 he was appointed chief of the telegraph office and in 1896 assumed the duties of train dispatcher. He was prominent in Great Northern Railway circles until his retirement in 1939. During World War II he was recalled to teach telegraphy and Morse Code. His 2 brothers were also employed by the Great Northern Railway for all their working years. The combined services of the 3 brothers were given special recognition by the railroad.

Lillian's parents were very active in community life, church, education, and politics in Great Falls. As was true of many who lived in the "wide open spaces" of the West, distances meant little to the Mayers. It was common, even in those days, for the family to travel 60 or 70 miles to fish or ride 135 miles to their ranch.

Their ranch, nicknamed "The Homestead," was situated in the Bear Paw Mountains. At the ranch everyone learned to ride horseback. Lillian recalls riding a horse 14 miles to her aunt's ranch to deliver a crock of butter. The family associations and early life established a partiality and enthusiasm for the Midwest and the West. Consequently in later life, the family made frequent trips to Montana, Oregon, Washington, and

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L. F. RICHDORF *is retired associate clinical professor of pediatrics, University of Minnesota, Minneapolis.*

California—though they also visited the eastern part of the United States. What the West meant to the family was to be enhanced by the interest in history on the part of the man Lillian married. Dr. Leo was an avid reader, particularly of the "Wild West."

This was the West—the land depicted by cowboy artist Charlie Russell, who for many years lived in Great Falls. His home was only a few blocks from that of the Mayer family.

Coupled with enthusiasm for the West was a desire for education. Lillian and her 2 sisters (an only brother died in infancy) made excellent records in grade and high school, then enrolled and graduated from the University of Minnesota. Valerie, the youngest, majored in social service, and Virginia (Jean) in English. Virginia, now Mrs. Rae Liebeler of Minneapolis, has taught English at the University of Minnesota and made contributions as a writer. Valerie married Ernest Lister and now resides in Eugene, Ore.

There was no medical school in the Northwest at the time Lillian entered the University of Minnesota in 1914. She was 16 years of age and the youngest in her class. Extracurricular activities were very much a part of her university life. She was good at tennis, canoeing, dancing, golf, and bridge. In medical students' parlance, she was a "good scout."

Other women in the premedic class included Helen McKeon, Helen Deane, Della Drips, Frances Ford, Gail Broberg, and Ruth Thygeson. In the fall of 1918, Rose Kriz and Ruth Boynton came to Minnesota from the University of Wisconsin. The scholastic ability of these women was high and the men in the class accepted them wholeheartedly, though good-natured joking was common. The few married students in the class were older men who were a fine influence on the unmarried medics. At least 2 of them, Charlie Flocken and Bill Foster, were outstanding in their fields before entering medical school. It should be mentioned that the University of Minnesota has always admitted women without restriction.

The university years were busy ones. Lillian's class of 1914 earned their B.S. degrees in 1918, M.B. degrees in 1920, and then became M.D.s in 1921. Most of her women classmates continued their education after completing their year as premedics. Several women, after obtaining their M.D. degrees, went on to specialize—Frances Ford in X-ray, Helen McKeon in anatomy, and Della Drips in obstetrics and gynecology. Dr. Ruth Boynton, a friend and associate of Lillian's for many years, later became director of Student Health Services at the University of Minnesota. In short, this class exemplified the ability of women and importance of their role in medicine.

After graduation in 1921, Lillian became associated with the Dr. Charles Granger Clinic of Rochester, Minn. In good weather the clinic doctors traveled by automobile to visit their patients, but during winter months their frequent 15- to 20-mile trips were made by a horse-drawn sleigh.

The attitude of the public toward women in medicine was not always as tolerant as that of her classmates in medical school. Lillian recalls a rather tragic but comic episode. In making a call she was met at the door by the wife of the man who was ill. After being challenged and questioned for some time as to her being a bona fide doctor and associate of Dr. Granger's, the wife allowed that "Dr. Lillian might as well come in," inasmuch as she was sure that "her husband was dead anyway." Needless to say, Dr. Lillian was amused rather than upset and chalked this up to experience. The incident illustrates the reluctance of the public to accept a "lady doctor."

The following year, 1923, Dr. Lillian was accepted at the Mayo Clinic as a fellow in the department of pediatrics. She spent a profitable year with that excellent clinician, Dr. Henry Helmholz, and his life-long friend and associate, Dr. Sam Amberg.

Nevertheless, she was not to continue in pediatrics. Her classmate, Dr. Ruth Boynton, requested that she return to the University Health Service as staff physician, which she did in 1924.

This return to Minneapolis made possible the renewal of an acquaintance with a young doctor, Leo Fink, a graduate of the University of Minnesota and Carleton College, who was interning at University Hospital.

On Thanksgiving Day, Nov. 26, 1925, Dr. Lillian and Dr. Leo (as everyone came to know them) were married at St. Lawrence Church near the university campus. "Women in medicine" attending the memorable occasion were Drs. Frances Ford, Della Drips, and Marbry Duryea. Other doctors attending were the groom's brother and "best man," Dr. Walter Fink, Dr. and Mrs. Neil Dungay, mutual friends of the bride and groom; also present were Mr. and Mrs. Leonard Furst of Little Falls, mentioned because of the lifelong friendship.

Following their marriage the Finks spent several years in New York and Philadelphia where Dr. Leo did graduate work in eye, ear, nose, and throat. After the graduate work was completed the couple returned to make their home in Minneapolis. Dr. Lillian continued doing some medical work but the rearing of their children soon became her primary objective.

The education of the children became a decisive factor. Round table discussions were routine in the Fink home. All participated in a lively manner on medical or current topics. The children had the example of their parents in freely expressing their opinions. Every opportunity of education was made available according to their temperaments and desires. All attended the University of Minnesota.

This schedule would have occupied most people's time—but not Lillian's. She became active in almost every organization in university circles. She accepted the presidency of the Alumna Club in 1940, served on the board of directors of the Alumni Association, and as treasurer of the American Association of University Women from 1944-1946. She was president of the Women's Auxiliary of the Hennepin County and State Medical societies in 1949 and 1963, respectively, and was president of Alpha Iota corporation in 1953.

In political areas she was a member of the Mayor's Committee for Revision of Edina Government in 1953, served on the family life committee of the Governor's Conference on Youth in 1955, and on the wage advisory board of the State Industrial Commission in 1956.

There was no facet of life in which her combination of an excellent memory and generous interests was not in evidence. She was interested in the Newman Club at the university and served as president of its Catholic Women's Guild from 1955-1957. Her interest in hospital work led her to accept the presidency of St. Mary's Hospital Auxiliary in 1962.

In each of these worthwhile projects she exemplified wholehearted cooperation with others. Many were aware of her work in only a particular organization and were surprised that anyone could have such broad interests, yet contribute so much to each group. There was always reflection and decision as to what was best to do and good judgment in selection of those people most able to help. Lillian was quiet and deliberate, and her concern was not for herself but for worthwhile projects.

Often she had letters to write, trips to make, and people to see. These she sandwiched in with her duties relative to her home and children. Time was used, plans were made, and what was accomplished reflected the "valiant woman." Perhaps it was a trip to North Dakota to care for the home while a daughter had a cesarean section, or to babysit when another daughter had a new baby, or again to see and take a grandchild to the doctor. Certainly her pediatric training was put to use. She was always clear-cut in her description of an illness that occurred in her family. She was always cooperative with the doctor, always prompt, giving her children and grandchildren the advantage of medical attention and hospital care. When she made suggestions to the consulting doctor, it behooved him to listen.

One episode comes to mind when a two-year-old grandchild sustained an injury. An examination to ascertain location of the injury was narrowed down to one leg, apparently the hip. An X-ray of the hip showed no injury, but Dr. Lillian suggested an X-ray be made of the lower femur, where the fracture was demonstrated.

This attention to her family was just taken for granted. There are 13 grandchildren of 2 married daughters. The third daughter has recently married, and a son, Bill, is at home after extensive work at the university.

Indeed, her work has just started, and our hats are off to a scholar, doctor, mother, educator, and citizen who is loyal to each facet and organization of her life experience. The little here delineated reflects only to a minor degree her capacity to make friends because she is such a good friend. Her constancy in work and organization, her ability to turn from one endeavor to another, her ability to recall circumstances and faces, and to make decisions with continuity—these qualities speak for efficiency under stress, and above all, the valiant woman.

Her ideas were related to her experience—whether in medicine, in community affairs, with her family, or in the home; first as a mother and now as a grandmother.

The grief suffered at the loss of a child had an effect on her ideas in pediatric care thereafter. Early care, prevention of a calamity, and hospitalization to protect the child were the wise concerns of the doctor and young mother.

The needs of her daughters and their children were always kept in mind. Beyond that were the needs of the community to provide family care when the parent, especially the mother, was incapacitated.

In a sense, pediatrics, internal medicine and allergy, as well as student health work, were her medical interests. But her work centered around the home, whether in health, education, or religion. Never did she lose sight of the fact that she was a doctor and the wife of a doctor.

Book Reviews . . .

A Doctor Talks to 9-to-12 Year Olds

by MARION O. LERRIGO *in consultation with* MICHAEL A. CASSIDY, *112 pp. (75 pp. insert 27 pp.) ill., Budlong Press, Chicago, 1964. $1.50*

This paperback book presents a comprehensive story of human development from conception through early puberty. It is accompanied by a supplement which gives advice to parents of children in the 9- to 12-year age bracket concerning their relationship with their children, as well as how to utilize the book.

In my opinion the book fulfills its purpose adequately. My only criticism is that it covers too much territory, not all of which is entirely pertinent. This may tend to dilute or detract from the interest or value to most readers. For example, fetal development and childbirth are intensely interesting to everyone, but I doubt whether the majority of children want to read about the various stages of development of the infant and child during the early months and years of life.

I also have some question about the pertinence of the advice concerning masturbation for the preteen-ager. Although masturbation is undoubtedly very common, it almost seems that children are being advised that it is so common as to be a routine habit, and that not to do it would seem somewhat abnormal. This portion could better be modified or incorporated in a book for older teenagers.

In recommending this book to his patients, a physician might be well-advised to point out the chapters which he considers of greatest value. There is much good information and advice for both children and parents.

L. G. PRAY, M.D.
Fargo

Treatment of the Aging Skin and Dermal Defects

by PERRY A. SPERBER, M.D., *105 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $5.75*

In the foreword of his monograph the author states that his purpose in writing was to fulfill the many requests which he had received from physicians in Europe, Asia, and the United States for more detailed information on the therapeutic use of chemexfoliation (chemosurgery) and silicone implantation.

A brief but interesting history of cosmetologic procedures from crude beginnings among the ancient Egyptians to the present period is presented. This is followed by a discussion of aging in general, including influences by the nervous system, endocrine factors, and genetics. Special reference is made to the aging skin. Changes caused by physical factors are considered, as well as chemical and physiological changes, water balance, cutaneous respiration, actual diseases of the skin, and topical therapy for aging skin.

Another chapter is devoted to facial plastic surgery for the aging skin. Surgical procedures for face lifting (rhytidectomy) and blepharoplasty are included, along with illustrations demonstrating methods for correction of sagging of the face and eyelids and removal of facial and neck wrinkles. Also discussed are methods and formulas for performing chemexfoliation, as well as detailed steps in carrying out the method for treating aging skin and acne scarring. The final presentation deals with silicone implantation, including the use of prosthetic liquid silicones to correct deep facial lines, wrinkles, hollows, furrows, depressions, and asymmetry.

The book can be recommended especially for dermatologists and plastic surgeons.

CARL W. LAYMON, M.D.
Minneapolis

Clinical Anticoagulant Therapy

by I. MYRON VIGRAN, M.D. *(with 8 contributing authors), 315 pp., ill., Lea and Febiger, Philadelphia, 1965. $15*

This book by Dr. Vigran is the culmination of his twenty years of experience with anticoagulant therapy. As one reads it, one realizes that the author is completely convinced that this form of therapy is essential in the proper treatment of vascular diseases today. Some clinicians and investigators may wonder whether one is justified in using anticoagulants in certain situations. Dr. Vigran wonders whether one is justified in withholding anticoagulants in these situations.

The bibliography in this book is extensive and complete. The author draws from the experiences of many clinicians and research workers in presenting and developing his subject. One has the feeling that those antagonistic to anticoagulation are given a less than deserved amount of space, and yet their views are quoted and discussed. The author has chosen as collaborators people whose views coincide with his. The foreword is written by Dr. Irving S. Wright, whose conviction of the value of anticoagulation is well known.

The first third of the book is devoted to the chemistry, physiology, and mechanics of clotting; the pathology of the involved vessels; the chemical and pharmacologic properties of the drugs used; and the laboratory tests used in the control of therapy. The book then becomes, and remains, wholly clinical as its name implies. Throughout the book the relative merits of heparin and the oral anticoagulants are discussed. The author also emphasizes the importance of properly instructing the patient. He should be cautioned regarding complications and advised of the necessity for keeping records.

The use of anticoagulants in the treatment of coronary artery disease is, as one would anticipate, the largest single section of the book. Detailed treatment of the acute and "impending" infarct, as well as the prophylaxis of recurrent myocardial infarction are given. The use of anticoagulants in pulmonary embolism and infarction and in cerebral vascular disease is also given in a fairly detailed manner. Beyond this, the use of anticoagulant drugs in lesser conditions is spelled out.

The final section of the book is devoted to a discussion and description of the complications of anticoagulant therapy, and is very complete. In the early part of the book, the contraindications to the use of these drugs are spelled out in detail and are divided into absolute and relative contraindications. Needless to say, if contraindications are kept in mind, the incidence of complications is much reduced.

The book is well written, printed in very easy-to-read form, and contains a great many tables which summarize the points the author wishes to stress. Italics are used very liberally throughout the book for emphasis. The book is decidedly clinically oriented and lives up to its title.

This is not a book which adds a great deal to the knowledge of the sophisticated cardiovascularly oriented physician, and its purpose is not really to do this. It is, as the author emphasizes, meant to serve as a practical guide to the use of anticoagulants, to point out where and how they should be used, and to help prevent their misuse. It summarizes the literature and represents the accumulated experiences of a cardiologist who has been intimately involved in this field of therapy ever since anticoagulant drugs have been available.

This book should be of value to all physicians using these drugs, and particularly to those who have need to acquaint themselves thoroughly with this form of therapy before using it. It should be helpful to the intern or resident in his training; he will find in one book all the facts he needs to know in applying intelligently this form of therapy.

MILTON M. HURWITZ, M.D.
St. Paul

Management of Emotional Problems of Children and Adolescents

by A. H. CHAPMAN, M.D., *315 pp., J. B. Lippincott Co., Philadelphia, 1965. $9.50*

This short, quite comprehensive book can be of great value to a practitioner, either one in general practice or in pediatrics. It is clearly and quite simply written and logically construed.

The author has divided his subject into 4 parts: *The healthy child.* This deals with the general emotional needs of children from birth through adolescence and the common sense care of these needs, giving a compact discussion of problems which frequently arise but can be considered normal, with advice on how the practitioner can handle them.

A survey of the emotional disorders of childhood. An approach to the management of some of them by the pediatrician and the family physician. Herein are discussed the development and symptoms of different disorders, with a most helpful differentiation between the phases which can be handled by the practicing physician and those which need special child guidance referral.

Evaluating and counseling children and parents. Techniques for the pediatrician and the family physician. Of particular value is the exposition of the different techniques of approach for different age groups. These are based on sound acquaintance with the progress of children's normal social reactions from birth through adolescence.

The clinical specialty of child psychiatry, its treatment methods and scope. In addition to a brief description of the workings of a child guidance clinic, there is included a chapter on the nature and treatment of psychoses of childhood and adolescence. For the practitioner this is the valuable section of Part 4 of the book, in that it is quite definitive about the true phychoses which, although rare, exist and need to be recognized.

The physician whose work involves the general care of children and adolescents will find this an excellent reference book because it gives unusually clear guidelines for behavior difficulties, normal and abnormal. If it is not scientifically profound and is somewhat repetitive, it is concise, definite, easy to refer to—due to its precise outline and reference index—and fulfills quite completely its stated purpose, not to be a scientific textbook on juvenile psychiatry, but to be "a clear, simple guide to the emotional disorders of childhood and adolescence."

ELIZABETH C. LOWRY, M.D.
Minneapolis

Counseling in Marital and Sexual Problems

edited by RICHARD H. KLEMER, PH.D., *309 pp., The Williams & Wilkins Co., Baltimore, 1965. $9.75*

As this well written and sensible book points out, about two-thirds of all physicians approaching practice have received no training in medical school, internship, or residency on how to deal with marital maladjustment. Yet the public somehow looks upon doctors as experts in this field and consults them more often than any other professional group when a marriage begins to fail. That the results are not always good is not surprising. This book is designed to help the physician correct this hiatus in his training. It is well written and well organized to accomplish this purpose.

Much of this book seems to me just the sort of common sense on marriage that one picks up bit by bit in the process of living and practicing medicine. Thus it should help the young physician to learn quickly what many of us have had to learn by slow trial and error. In addition, it has many more subtle insights into the causes and effects of marital problems which could sharpen the more experienced physician's approach to patients with this kind of difficulty. Dr. Klemer has written about one-third of the pages himself and has managed to coordinate the efforts of the impressive array of medical and nonmedical marriage experts on the rest of the book so that it makes a meaningful whole. I can think of no problems in marriage counseling which I have met in practice that are not effectively discussed in this book.

As a handbook it should help the physician marriage counselor in 2 ways:

1. To improve his technique in dealing directly with ailing marriages on such diverse problems as deciding who must see the psychiatrist, what is sexual incompatibility, sexual deviations, premarital and extramarital pregnancy, marital infidelity, sex in older patients, the climacteric years, parent-child problems, alcoholics, the overdominant partner, and infertility.

2. To improve the doctor's understanding of those psychosomatic illnesses and complaints which have roots in an unhappy marriage about which the patient is too reticent or embarrassed to talk. I particularly liked the chapters by Dr. Klemer on male sexual conditioning, female sexual conditioning, and talking with patients about sexual problems.

It is refreshing in a day of "new morality" when even some parsons seem about ready to repeal the Ten Commandments to run into authors who believe there ought to be some inhibitions and rules about sexual behavior for the good of the people concerned. While being far from legalistic, the authors doubt if modern society is right in making "cataclysmic orgasm—the ultimate test of feminine achievement" and quote sympathetically the opinion of a 22-year-old woman student who said: "Parents must teach their children in such a way that they will not want to go counter to what they believe to be right and just and good. Done this way, taboos become willful self-restraints."

All in all, I recommend this book to the busy, practicing physician who feels that he needs to know more about how to fix ailing marriages, or more importantly, how to treat patients suffering basically from such marriages.

KRISTOFER HAGEN, M.D.
Minneapolis

The Pediatric Patient 1965

edited by SARAH R. GUSTAFSON, PH.D., *and* DAVID BAIRD COURSIN, M.D., *216 pp., ill., J. B. Lippincott Co., Philadelphia, 1965. $6*

This is one of a seemingly inexhaustible number of books which attempt to keep the practicing pediatrician up to date on recent advances. It should appeal both to the practitioner who wishes to extend his theoretic knowledge of the esoteric as well as the busy man who just wants to know of recent practical advances.

The first chapter on immunology is well worth the effort involved in reading and rereading in order to become acquainted with the terminology of immunologists. While there may be relatively few immediate applications of the theories propounded, even an imperfect understanding will reward the clinician in his personal attempt to "keep up with the literature."

The chapter on allergy has a good review of the controversial milk antibody as a cause of sudden death.

The newborn chapter has a good review on the management of the respiratory distress syndrome. A chapter on new syndromes describes a few of the newer inborn errors of metabolism.

The review of adolescence may stimulate the practitioner's interest in a field which is just "coming into its own."

The miscellany chapter is just what its name implies. I am sure the suggestion by Schapiro that proctologic examination be done routinely in children will not find much favor, either with the children or with the pediatrician.

The illustrations are well done. The paper and printing are average.

I believe this book will reward the practitioner well for any time he spends digesting it.

STUART LANE AREY, M.D.
Minneapolis

Physiologic Foundations for Marriage Counseling

by JOSEPH B. TRAINER, M.D., *287 pp., ill., C. V. Mosby Co., St. Louis, 1965. $8*

This textbook on a vital subject in a field that is being increasingly included in the medical school curriculum is written by the Director of Health Services and an assistant professor of physiology and medicine of the University of Oregon Medical School. The dual nature of the author's background helps explain why the book displays such an interesting combination of physiological detail and practical common sense about one of life's most fascinating subjects—sex and mating. At times, the author sounds like the precise professor of physiology lecturing to his class and, then again, like the practicing physician making offhand, slightly brash remarks to patients who have come for advice. In general, the book seems accurate and objective enough to call it a textbook, and since its field is so new it will probably fill a felt need, at least as a reference.

One of the chief values is the inclusion at the end of each chapter of a list and evaluation of references on the subjects discussed. Since the chapters include such a helpful variety of subjects (the evolutionary development of human reproduction, sex and the nervous system, male hormones and man, male psyche meets woman, female hormones and women, mating, pregnancy, intersex, contraception, infertility, abortion, fatigue in marriage, and premarital examinations) the references become a great help to the serious student in the field.

Probably the most helpful chapter in the book is the one on medical genetics and developmental defects, a subject of intense importance to the physician advising couples on future pregnancies where doubt exists about their genetic background. The author draws heavily on the excellent book, *Counseling in Medical Genetics* by Sheldon C. Reed, a recent contributor to this mushrooming field of knowledge. Another topic of value, not only for the marriage counsellor but also for the practicing physician, is on tired wives and husbands. He wisely points out that fatigue in general is often the result of the "calamity of idleness," while goals may energize. In his physiology of fatigue, I appreciated the simple explanation of how monoamine oxidase inhibitors work and how they differ from direct central nervous system stimulants.

Aside from injection of certain religious-based ideas with which I do not agree, the work is a needed textbook and should be in every medical school library and on the shelves of every medical office or clinic where any considerable marriage counseling is done.

KRISTOFER HAGEN, M.D.
Minneapolis

A Short Textbook of Haematology

by R. B. THOMPSON, M.D., *2nd. ed., 350 pp., ill., J. B. Lippincott Co., Philadelphia, 1965. $7.50*

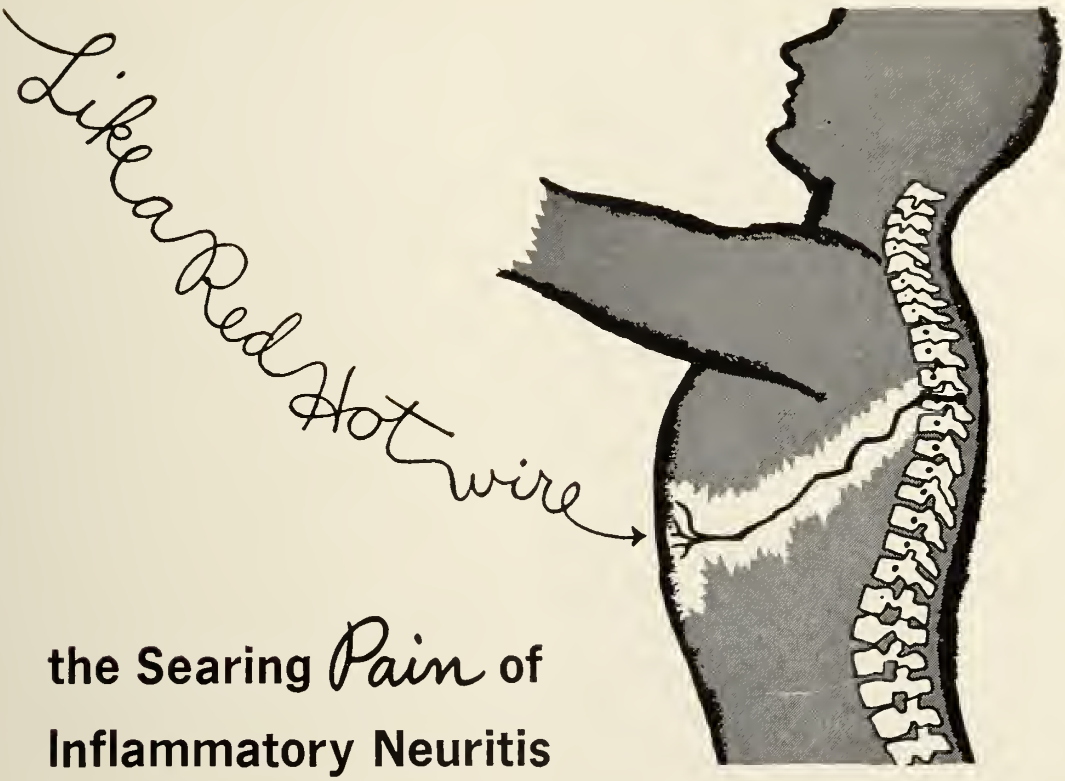
The second edition of "Short Textbook of Haematology" by a British physician, R. B. Thompson, and published in this country by J. B. Lippincott, is a short, generally excellent textbook on hematology. Written primarily for practicing general physicians and senior students, it surveys the field quite broadly and yet is sufficiently detailed to satisfy the needs of those looking for a practical exposition of specific blood problems. References included in each section are few, but in general they are adequate for key review material.

The author's language is simple, direct, and personal in flavor. The opinions expressed seem reasonable and authoritative. Organization is excellent and grouping of material such as hypochromic, hyperferremic anemias, miscellaneous anemias associated with metabolic disorders, and general disease is done in a manner which simplifies concepts of blood disorders with common or related features.

Therapy is outlined in sufficient detail to be generally useful. The reviewer finds some differences of opinion in choices and modes of therapy, but these are, for the most part, in areas of treatment of hematologic malignancies where there is plenty of room for difference of opinion.

For readers who want quick reference, short review appraisal, and up-to-date information of a rather general nature on hematologic subjects, this book fills the bill very well and can be enthusiastically recommended.

ROBERT A. GREEN, M.D.
Minneapolis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References: (1) Baker, A. G.: Penn. Med. J. *63*:697-698 (May) 1960. (2) Smith, R. T.: New York Med. *8*:16-19 (Aug. 20) 1952. (3) Smith, R. T.: Med. Clin. N. America (March) 1957. (4) Lehrer, H. W.; Lehrer, H. G., and Lehrer, D. R.: Northw. Med. *54*:1249-1252 (Nov.) 1955. (5) Sforzolini, G. S.: Arch Ophthal. *62*-381-385 (Sept.) 1959. (6) Shupala, E.: W. Virginia Med. J. *56*:191-193 (June) 1960. (7) Xander, G. W.: Western Med. *1*:14-17 (Sept.) 1960. (8) Combs, F. C., and Canizares, O.: New York J. Med. (Mar. 15) 1952, pp. 706-708. (9) Marsh, W. C.: U.S. Armed Forces Med. J. *1*:1045 (Sept.) 1950. (10) Love, T. R.: Rocky Mountain Med. J. *50*:873 (Nov.) 1953.

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BOOK REVIEWS

(Continued from page 158)

Chemistry and Prevention of Congenital Anomalies

by HIDEO NISHIMURA, M.D., *119 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $5.75*

This monograph will be a valuable addition to the libraries of those scientists interested in an exhaustive and superb bibliography dealing with the subject of congenital malformations. Included are such topics as environmental factors as metabolic inhibitors, possible teratogens in man, and nongenetic maternal conditions associated with human anomalies.

The chapter dealing with the prevention of abnormalities is too brief and incomplete. The illustrations are clear and precise and the book reads easily. The material is presented in concise fashion and is well organized.

The monograph will not appeal to the average student of medicine nor physicians but will undoubtedly be studied by researchers and others who are investigating congenital malformations in man.

FRED A. LYON, M.D.
Minneapolis

Gynecology

edited by ROBERT A. KIMBROUGH, M.D., *619 pp., ill., J. B. Lippincott Co., Philadelphia, 1965.*

Dr. Kimbrough, along with many outstanding collaborators, has produced a new textbook on gynecology which is bound to be one of the outstanding books in its area of concern. The content reads very easily, the illustrations are of superb quality, and the overall appearance of the book is excellent. Dr. Kimbrough has chosen various experts in the field of obstetrics and gynecology to write each appropriate chapter in the textbook. Of particular interest to the student of medicine, as well as to the practitioner, is the fact that the book contains an excellent chapter on embryology and congenital malformations. The most recent advances in gynecology are included in this book, with references that are up to date.

A chapter entitled "Psychosomatics in Gynecology" will be of great help to the practitioner. It contains much valuable information which will benefit all physicians dealing with the female patient.

This book is highly recommended to anyone interested in purchasing a textbook of gynecology. Dr. Kimbrough is to be commended for choosing the eminently qualified physicians who collaborated with him in the publication of this new book.

FRED A. LYON, M.D.
Minneapolis

Burns: A Symposium

edited by LEON GOLDMAN, M.D., *and* RICHARD E. GARDNER, M.D., *191 pp., Charles C Thomas, Publisher, Springfield, Ill., 1965. $7.75*

"Burns: A Symposium," edited by Drs. Leon Goldman and Richard Gardner of the Department of Surgery at the University of California School of Medicine, is a verbatim record of the panel discussions by nationally known authorities from the largest burn centers in this country. Included in this group are Drs. J. Barrett Brown and Carl Moyer of Washington University, Stephen R. Lewis of the University of Texas, Nicholas Georgiade of Duke University, Col. John Moncrief of Brooke Army

Medical Center, and others. Since this book is a dialogue between surgeons and research scientists with a special interest in burns, a practicing physician would need a good background in the care of major burns in order to gain anything from it. As one might suspect, many of the ideas presented are controversial. Although Dr. Carl Moyer was a participant in these sessions, there is no mention of his new silver nitrate treatment which may revolutionize thinking on care of the burn wound. In conclusion, the book has very limited appeal.

WALTER L. LYNN, M.D.
Minneapolis

NEW BOOKS RECEIVED

Surgery: Principles and Practice by CARL A. MOYER, M.D., JONATHAN E. RHOADS, M.D., J. GARROTT ALLEN, M.D., and HENRY N. HARKINS, M.D., 3rd ed., 1,828 pp., ill., J. B. Lippincott Co., Philadelphia, 1965. $18

Cerebral Edema by LOUIS BAKAY, M.D., and JOSEPH C. LEE, M.D., 192 pp., ill., Charles C Thomas, Publisher, Springfield, Ill., 1965. $9.75

Aspects of Anxiety with a preface by C. H. HARDIN BRANCH, M.D., 80 pp., ill., J. B. Lippincott Co., Philadelphia, 1965. $3.50

A Primer of Peripheral Vascular Diseases by TRAVIS WINSOR, M.D., and CHESTER HYMAN, PH.D., 348 pp., ill., Lea & Febiger, Philadelphia, 1965. $12.50

Plastic Surgery of the Nose: Including Reconstruction of War Injuries and of Deformities from Neoplastic, Traumatic, Radiation, Congenital, and Other Causes (Revised Second Printing) by JAMES BARRETT BROWN, M.D., and FRANK MC DOWELL, M.D., 432 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $21

The Practice of Psychoanalytic Psychotherapy by MARC H. HOLLENDER, M.D., 156 pp., Grune & Stratton, New York City, 1965.

Chromosome Diagnostics in Clinical Medicine by ROBERT R. EGGEN, M.D., 347 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $12.50

Surgery of the Foot by HENRI L. DU VRIES, B.S., 2nd ed., 586 pp., ill., C. V. Mosby Co., St. Louis, 1965. $17.50

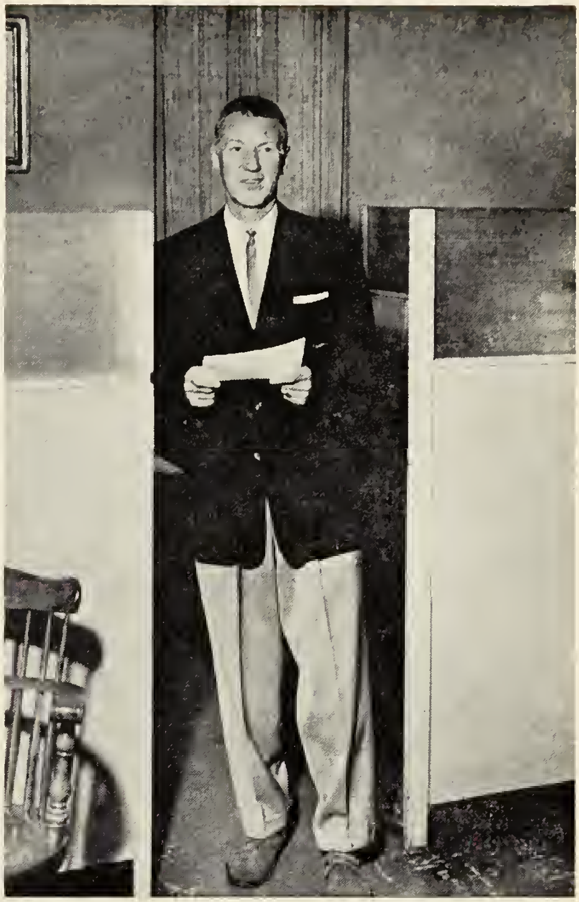
Respiratory Care by H. H. BENDIXEN, L. D. EGBERT, J. HEDLEY-WHYTE, M. B. LAVER, and H. PONTOPPIDAN, 252 pp., ill., C. V. Mosby Co., St. Louis, 1965. $15

Radiologic Diagnosis in Infants and Children by ARMAND E. BRODEUR, M.D., 503 pp., ill., C. V. Mosby Co., St. Louis, 1965. $26.50

The Chest Film in Massive Pulmonary Embolism by DANIEL J. TORRANCE, JR., M.D., 74 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $6.75

Behavior, Aging, and the Nervous System edited by A. T. WELFORD, M.A., and JAMES E. BIRREN, PH.D.,

(Continued on page 18A)



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(Continued from page 17A)

637 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $22.50

Diagnosis and Therapy of the Glaucomas by BERNARD BECKER, M.D., and ROBERT N. SHAFFER, M.D., 443 pp., ill., C. V. Mosby Co., 1965. $18.50

Cardiac Evaluation in Normal Infants by ROBERT F. ZIEGLER, M.D., 170 pp., ill., C. V. Mosby Co., St. Louis, 1965. $12.75

An Introduction to General Virology by THOMAS M. BELL, B.SC., 284 pp., ill., J. B. Lippincott Co., Philadelphia, 1965. $7.50

Symposium on the Lens sponsored by Visual Sciences Study Section and University of Minnesota, JOHN E. HARRIS, chairman, 381 pp., ill., C. V. Mosby Co., St. Louis, 1965. $18.50

A History of Ophthalmology at the University of Pennsylvania by DANIEL M. ALBERT, M.D., and HAROLD G. SCHEIE, M.D., 388 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $13.50

Advances in Blood Grouping, Volume II by ALEXANDER S. WIENER, M.D., with a section by MAURICE SHAPIRO, M.B., 454 pp., ill., Grune & Stratton, New York, 1965. $12.50

Progestogen Therapy by MAXWELL ROLAND, 88 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $9

The Electrocardiogram and Vectorcardiogram in Congenital Heart Disease by MARIO R. GARCIA-PALMIERI, M.D., ROBERTO C. RODRIGUEZ, M.D., and CARLOS E. GIROD, M.D., 123 pp., ill., Grune & Stratton, New York City, 1965. $6.50

Vitreoretinal Pathology and Surgery in Retinal Detachment by PAUL A. CIBIS, M.D., 293 pp., ill., C. V. Mosby Co., 1965. $20.00

Current Problems in Tuberculosis by SAMUEL PHILLIPS, M.D., 123 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $7.50

Injuries of Nerves and Their Consequences: American Academy of Neurology Reprint Series by S. WEIR MITCHELL, M.D., 377 pp., Dover Publications, Inc., New York, 1965. $2.75

Symposium on Cataracts: Transactions of the New Orleans Academy of Ophthalmology by BENJAMIN F. BOYD, M.D., LEONARD CHRISTENSEN, M.D., A. RAY IRVINE, JR., M.D., MURRAY F. MCCASLIN, M.D., P. ROBB MCDONALD, M.D., JOHN M. MCLEAN, M.D., and RICHARD C. TROUTMAN, M.D., 340 pp., ill., C. V. Mosby Co., St. Louis, 1965. $19.50

Heart Disease in Children: Diagnosis and Treatment by BENJAMIN M. GASUL, M.D., RENE A. ARCILLA, M.D., and MAURICE LEV, M.D., 1,363 pp., ill., J. B. Lippincott Co., Philadelphia, 1966. $33

Neurocutaneous Diseases by JOHN A. AITA, PH.D., 85 pp., Charles C Thomas, Publisher, Springfield, Ill., 1965. $4.75

The Burn Wound by CAPTAIN STANLEY E. ORDER, M.D., and COLONEL JOHN A. MONCRIEF, M.D., 72 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $7.75

Fifth National Cancer Conference Proceedings, 1964 sponsored by THE AMERICAN CANCER SOCIETY, INC., and NATIONAL CANCER INSTITUTE, 764 pp., ill., J. B. Lippincott, Philadelphia, 1965. $10

Therapeutic Radiology by WILLIAM T. MOSS, M.D., 2nd ed., 524 pp., ill., C. V. Mosby Co., St. Louis, 1965. $18.75

Neurohistochemistry edited by C. W. M. ADAMS, M.A., 753 pp., ill., American Elsevier Publishing Company, New York, 1965. $29

Applied Hypnosis and Positive Suggestion in Medicine, Dentistry and Patient Care by GEORGE A. ULETT, B.A., and DONALD B. PETERSON, M.D., 134 pp., C. V. Mosby Co., St. Louis, 1965. $8.50

Caries Resistant Teeth edited by G. E. W. WOLSTENHOLME and MAEVE O'CONNOR, Ciba Foundation Symposium, 338 pp., ill., Little, Brown & Co., Boston, 1965. $12.50

Colour Vision: Physiology and Experimental Psychology edited by A. V. S. DE REUCK and JULIE KNIGHT, 382 pp., ill., Little, Brown & Co., Boston, 1965. $12.50

Diuretic Therapy: An Appraisal of Diuretic Drugs edited by ARTHUR C. DE GRAFF, M.D., and ALAN F. LYON, M.D., 41 pp., C. V. Mosby Co., St. Louis, 1965. $3.50

The Doctor and His Patient: A Sociological Interpretation by SAMUEL W. BLOOM, PH.D., 268 pp., ill., The Free Press, New York City, 1965. $1.95

Drug Presentation and Prescribing by W. R. L. BROWN, PH.D., and J. W. HADGRAFT, 118 pp., ill., Pergamon Press, New York City, 1965. (paper)

The Keys to Orthopedic Anatomy by WILLIAM A. MILLER, M.D., 155 pp., Charles C Thomas, Publisher, Springfield, Ill., 1965. $5.75

List of Fungal Products by SHOJI SHIBATA, SHINSAKU NATORI, and SHUN-ICHI UDAGAWA, 170 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $7.75

Refraction: A Programmed Text by ROBERT D. REINECKE, M.D., and ROBERT J. HERM, M.D., 336 pp., ill., Appleton-Century-Crofts, New York City, 1965. $12.50

The Search for Sanity by S. LEFF, and V. LEFF, 146 pp., Pergamon Press, Long Island, N.Y., 1965. (paper)

Twins: Twice the Trouble, Twice the Fun by BETSY HOLLAND GEHMAN, 224 pp., J. B. Lippincott Co., New York, 1965. $4.95

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News Briefs . . .

North Dakota

DR. RALPH J. DUNNIGAN has been elected chief of staff of St. Alexius Hospital, Bismarck. Other new officers are Dr. John B. Frankel, president-elect; Dr. Ralph E. Tarnasky, secretary; and Dr. Delano M. Pfeifle, member-at-large. Past president is Dr. Joseph W. Cleary.

* * * *

DR. MILTON O. BERG of Valley City has been elected president of the Sheyenne Valley Medical Association. Elected with him were Dr. Neil A. Macdonald, vice-president, and Dr. John W. Goven, secretary.

* * * *

DR. BERNARD A. GIRARD of Mandan has been elected a member of the American Academy of General Practice.

* * * *

DR. GALE R. RICHARDSON, pathologist, has been elected chief of staff at St. Joseph's Hospital, Minot.

* * * *

DR. JAMES R. BISHOP, Jamestown, has been elected a member of the American Academy of General Practice.

* * * *

DR. PETER W. S. PATTON, general practitioner from Essex, England, has established practice in Cooperstown in association with Dr. Kenneth M. Wakefield.

* * * *

DRS. C. M. ADLI and OMAR F. TURNACIOGLU have joined the staff of the Quain and Ramstad Clinic, Bismarck. Dr. Adli is a specialist in orthopedics and Dr. Turnacioglu in anesthesiology.

Minnesota

DR. GREGORY A. SCHISSEL, Crystal physician, has been named a member of the board of trustees of the St. Therese Nursing Home to be built in New Hope. Dr. Schissel will serve on the building committee.

* * * *

DR. J. GORDON BEATON of Farmington has been elected president of the medical staff of Northfield City Hospital.

* * * *

DR. RUSSELL C. POPOFF of Graceville has purchased the Oliver Clinic building and equipment from the Graceville Clinic Corporation. Dr. Popoff will continue to operate the Oliver Clinic as a private practice.

* * * *

TWO MAYO CLINIC PHYSICIANS, Drs. Joseph M. Janes and Charles G. Moertel, have received research grants from the Minnesota division of the American Cancer Society. Dr. Janes, an orthopedic surgeon, received $4,000, and Dr. Moertel, a gastroenterologist, $2,500.

* * * *

DR. LOIS ANN ANSELMENT of Excelsior has been elected a member of the American Academy of General Practice.

* * * *

DR. DONALD S. ASP, Milaca physician, has joined the staff of the Henry Clinic of Milaca, in association with Dr. Joseph E. Henry

* * * *

ELEVEN NEW SPECIALISTS have joined the staff of the Mayo Clinic, Rochester. Mayo graduate school residents in the group are Drs. Roger E. Cupps, appointed consultant in the section of therapeutic radiology; Charles C. Kennedy, consultant in internal medicine; Bruce A. Lund, consultant in the section of dentistry and oral surgery; Edward C. Rosenow III, consultant in internal medicine; Ronald J. Forth, consultant in internal medicine; Francoise M. Carney, consultant in anesthesiology; and Robert L. Scanlan, consultant in the section of diagnostic roentgenography. The other four appointees are Drs. Dan E. Tolman, consultant in the section of dentistry and oral surgery; Virgil F. Fairbanks, consultant in clinical pathology; James W. Linman, consultant in clinical pathology; and Albert L. Rhoton, consultant in neurologic surgery.

* * * *

DR. HENRY H. YOUNG, chairman of the Mayo Clinic orthopedic section, has been reelected to a fifth straight term as a vice-president of the Minnesota Safety Council.

* * * *

DR. HARRY FOREMAN, associate professor in the University of Minnesota school of public health, has been named associate dean of the university's office of international programs. Dr. Foreman will work on international education programs affecting or aided by the university.

* * * *

DR. HARRY J. WILLIAMS III, obstetrician from Flushing, N.Y., has joined the Medical Block Clinic in Red Wing. Dr. Williams is a Fellow of the American College of Obstetricians and Gynecologists and the American Society of Abdominal Surgeons.

* * * *

RESEARCH GRANTS TOTALING $77,000 were made recently to the University of Minnesota by Mr. and Mrs. Joseph Gales Ramsay of St. Paul. Dr. C. Walton Lillehei, professor of surgery, received $70,000 for research, fellowships, and a staff position in cardiovascular surgery. Dr. Owen Wangensteen, chairman of surgery, accepted a $5,000 grant for further development of a library of medical history. Miss Annie Laurie Baker, professor of social service, and Miss Margaret Stanchfield, senior social service worker, received $2,000 for social service work to be performed in the university hospitals.

* * * *

DR. JOHN P. SAVARYN has resumed the general practice of medicine in Waconia after a four-year surgical residency at the University of Minnesota and the Minneapolis Veterans Administration Hospital.

* * * *

DR. MYRON I. DOEBLER, Mora, has accepted a position as medical director of the Armour Company in St. Paul. Dr. Doebler will continue to live in Mora and serve part-time at the Mora Clinic.

* * * *

DR. BERNARD S. NAUTH, formerly of Minneapolis, has opened practice in the PBC Medical Clinic, Brooklyn Center.

* * * *

DR. GERALD E. COTTON of Fosston has been elected a member of the American Academy of General Practice.

* * * *

DR. JOHN L. MARSO, formerly of the Mankato Clinic, is now associated with Dr. George E. Penn of Mankato in the practice of obstetrics and gynecology.

(Continued on page 22A)

Low host resistance?

Consider the "extra" antibacterial activity of Ilosone®

Occasionally, therapeutic failure is due to the patient's inability to mobilize his defenses sufficiently to overcome infection. Typical of this is the debilitated patient, the premature infant, or the diabetic. It is in these patients that the high levels of antimicrobial activity of Ilosone are especially useful. Ilosone has demonstrated antibacterial levels two to four times those of erythromycin base or stearate. Furthermore, it attains them earlier and maintains them longer. Even the presence of food does not appear to affect the activity of Ilosone.

Contraindications: Ilosone is contraindicated in patients with a known history of sensitivity to this drug and in those with preexisting liver disease or dysfunction.

Side-Effects: Even though Ilosone is the most active oral form of erythromycin, the incidence of side-effects is low. Infrequent cases of drug idiosyncrasy, manifested by a form of intrahepatic cholestatic jaundice, have been reported. There have been no known fatal or definite residual effects. Gastro-intestinal disturbances not associated with hepatic effects are observed in a small proportion of patients as a result of a local stimulating action of Ilosone on the alimentary tract. Although allergic manifestations are uncommon with the use of erythromycin, there have been occasional reports of urticaria, skin eruptions, and, on rare occasions, anaphylaxis.

Dosage: *Children under 25 pounds*—5 mg. per pound of body weight every six hours. *Children 25 to 50 pounds*—125 mg. every six hours. *Adults and children over 50 pounds*—250 mg. every six hours. For severe infections, these dosages may be doubled.

Available in Pulvules®, suspension, drops, and chewable tablets. Ilosone Chewable tablets should be chewed or crushed and swallowed with water.

Ilosone®

Erythromycin Estolate

Additional information available to physicians upon request. Eli Lilly and Company, Indianapolis, Indiana. 501280

Lilly

(Continued from page 20A)

NEW FACULTY APPOINTMENTS at the Mayo Graduate School of Medicine, University of Minnesota, include: Dr. Jorge E. Maldonado, instructor in medicine; Dr. Robert Wallace, instructor in surgery; Dr. David K. Trites, associate professor of psychology; and Dr. Lillian R. Elveback, professor of biostatistics. The appointments, along with Dr. R. Drew Miller's promotion to professor of medicine, have been approved by the board of regents.

* * * *

DR. ROBERT R. KIERLAND, head of the dermatology section at the Mayo Clinic, has been elected the first president of the Dermatology Foundation, which was created late in 1965 to obtain support for educational and scientific activities.

* * * *

THE HENNEPIN COUNTY Board of Commissioners has authorized a 4-bed unit at General Hospital, Minneapolis, for the treatment of kidney diseases. Operational costs for three years are covered by a $143,000 federal grant.

* * * *

DR. JOHN T. KELLY is the new chief-of-staff at St. Marys Hospital, Minneapolis, succeeding acting-chief Dr. Walter F. Subby.

* * * *

DR. JOEL O. BRENDE of Taylors Falls has joined the Littlefork Medical Clinic.

* * * *

DR. CHARLES J. BECK has been elected chief-of-staff at St. Johns Hospital, St. Paul, succeeding Dr. Cyril R. Tifft.

* * * *

A SYMPOSIUM ON LIVER DISEASE is scheduled May 23 through 25 in the Mayo Auditorium of the University of Minnesota. Dr. John Murray, associate professor of medicine at the university, said the sessions are open to all physicians at no charge.

* * * *

DR. HENRY J. NOWAK, assistant to the Veterans Administration medical director in St. Paul, has been named director of the VA hospital at Spokane, Wash. Dr. Nowak received his degree from the University of Illinois College of Medicine in 1938.

* * * *

THE MINNEAPOLIS POST OFFICE has announced a vacancy for the position of Medical Officer. The beginning salary ranges from $11,599 to $14,632 per annum. Applicants must be citizens of the United States and graduates of an approved medical school, with a degree of doctor of medicine, and must be licensed to practice. Application forms may be obtained from the Board of Examiners, U.S. Civil Service Commission, Room 432, Main Post Office, Minneapolis, Minnesota 55401.

South Dakota

DR. EDWARD A. RUDOLPH, has been elected president of the medical staff of St. Luke's Hospital, Aberdeen. Dr. Albin J. Janusz was elected vice-president, and Dr. Roger A. Standard, secretary. These officers succeed Drs. Robert E. Bormes, Bernard F. King, and Carson B. Murdy, respectively.

(Continued on page 24A)

DEPROL®

meprobamate 400 mg. +
benactyzine hydrochloride 1 mg.

Indications: 'Deprol' is useful in the management of depression, both acute (reactive) and chronic. It is particularly useful in the less severe depressions and where the depression is accompanied by anxiety, insomnia, agitation, or rumination. It is also useful for management of depression and associated anxiety accompanying or related to organic illnesses.

Contraindications: Benactyzine hydrochloride is contraindicated in glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

Precautions: *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of preexisting symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

Benactyzine hydrochloride—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

Meprobamate—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Dosage: Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

Supplied: Light-pink, scored tablets, each containing meprobamate 400 mg. and benactyzine hydrochloride 1 mg.
Before prescribing, consult package circular.

WALLACE LABORATORIES / *Cranbury, N. J.*
CD-6952

FOR THE DEPRESSION ↔ INSOMNIA ↔ TENSION ↔ ANXIETY ↔ COMPLEX

TRY DEPROL® meprobamate 400 mg. + benactyzine hydrochloride 1 mg.

a logical first choice

FOR DEPRESSION

even when complicated by anxiety, tension, insomnia, agitation or rumination.

- Acts rapidly.
- Side effects at recommended dosage infrequent, usually easily controlled.

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RATES: 70 words or less, one time, $3, two consecutive times, $5. Copy must reach us by the 10th of the month preceding publication. REPLIES to advertisements with key numbers should be addressed in care of THE JOURNAL-LANCET, 65th at Valley View Road, Southdale Park, Minneapolis, Minnesota 55424.

WANTED—Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty-seven bed hospital with X-ray and laboratory technicians and nurse anesthetist. Good hunting and fishing. Adequate salary and time off. Contact A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

WANTED—1 or 2 general practitioners. Excellent clinic and hospital facilities. Rural practice established 18 years. Salary open, partnership if compatible. Lloyd H. Klefstad, M.D. Greenbush, Minn.

SACRED HEART, MINNESOTA has been without a doctor since 1961. General practitioner will find suitable building in 700 pop. village, modern hospital 10 miles away; progressive, stable community in west central part of state. Good school, churches. Good family environment. Call or write Rev. Robert Bardy, Telephone 765-2547, Sacred Heart, Minn.

FOR SALE—General Practice established fifteen years, Minneapolis suburban area in fully equipped new medical building. Full laboratory, X-ray. 400 bed hospital, five minutes away. Leaving for residency July 1966. Will introduce. Gross 150 M. Easy terms. Write Box 39 Journal Lancet, 65th and Valley View Road, Minneapolis, Minn. 55424.

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The skill of the maker and the fitter are of paramount importance. . . . We measure accurately, fit carefully, follow directions religiously.

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NEWS BRIEFS

(Continued from page 22A)

DR. PAUL R. LEON, of Aberdeen, has been elected president of the Aberdeen District Medical Society. Also elected were Dr. Karlis Zvejnieks, Leola, vice-president, and Dr. William R. Taylor, Aberdeen, secretary-treasurer. Dr. Edmond J. Perry, Redfield, is counselor to the South Dakota State Medical Society. Delegates to the annual meeting are Dr. Gerrit J. Bloemendaal, Ipswich, and Dr. Bernard C. Gerber and Dr. Paul G. Bunker, both of Aberdeen.

* * * *

DR. EBERHARD H. HEINRICHS has been elected chief of the medical staff of Watertown Memorial Hospital, succeeding Dr. Theodore J. Wrage, Jr. Other new officers are Dr. Charles F. Ryan, vice-president, and Dr. Gerald E. Tracy, secretary-treasurer. The staff executive committee will consist of the officers plus Dr. G. Robert Barton and Dr. H. Russell Brown.

* * * *

DR. JOHN B. GREGG of Sioux Falls has been named outstanding physician of the year in South Dakota by the Governor's committee on employment of the handicapped. He was cited for his work as a physician, a lecturer at the University of South Dakota Medical School, a contributor to medical journals, and a consultant to the Nu Voice Club of the American Cancer Society.

Deaths . . .

DR. RITA M. BRADY, 40, formerly of Devils Lake, N.D., died on Jan. 11 enroute to a hospital in Great Falls, Mont., where she had lived since 1961. Dr. Brady received her medical degree from Marquette University School of Medicine, Milwaukee, Wis., in 1950. She practiced radiology in Philadelphia and San Francisco until ill health forced her to return to Great Falls in 1961 to live with her father. She was a member of the American College of Radiology.

* * * *

DR. HARRY C. JENSEN, 70, owner of Edina Medical Center, Minn. and retired general practitioner, died Jan. 1 at North Miami Beach, Fla. Dr. Jensen received his medical degree in 1922 from the University of Minnesota.

* * * *

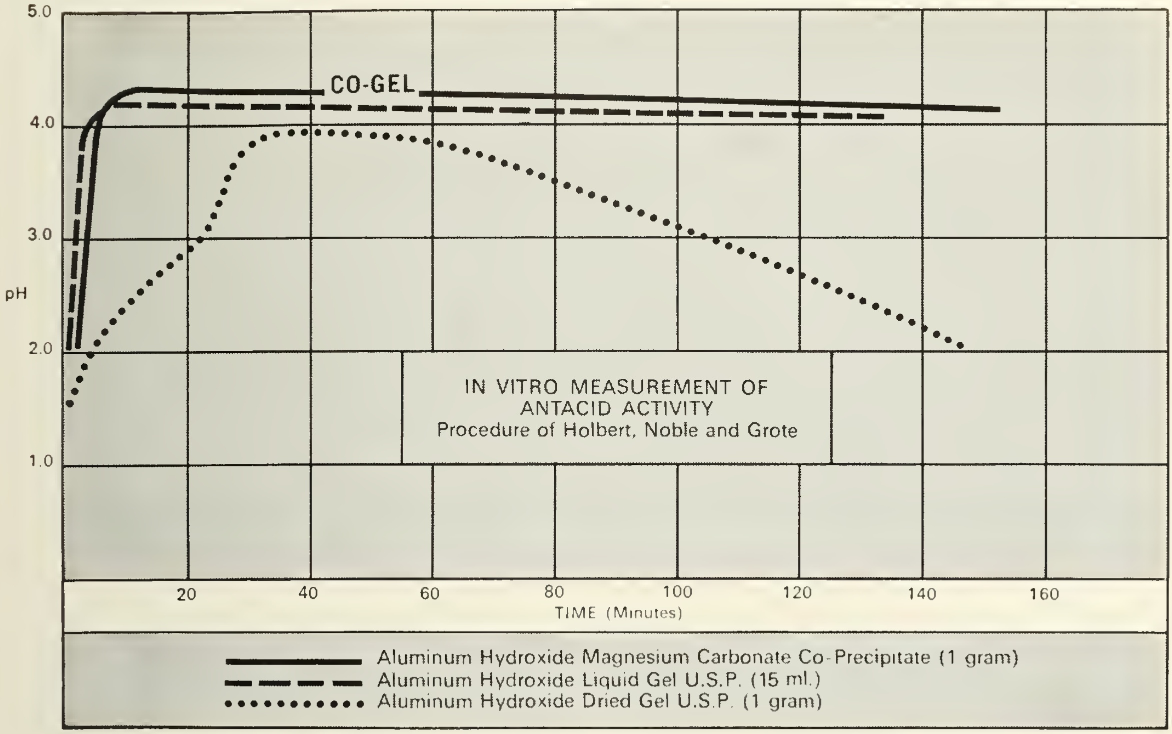
DR. ARCHIBALD O. OLSON, 65, ophthalmologist, died Jan. 6 in Duluth. Dr. Olson graduated in 1930 from Rush Medical College, Chicago, and was a member of the American Academy of Ophthalmology and Otolaryngology. He had practiced in Duluth since 1937.

* * * *

DR. ROGER L. J. KENNEDY, 68, pediatrician and former head of a section of pediatrics at the Mayo Clinic, died in Rochester, Jan. 14. Dr. Kennedy received his medical degree from the University of Minnesota in 1921 and was associated with the Mayo Clinic from 1923 until his retirement in 1961. He was a Fellow of the American Medical Association and the American Academy of Pediatrics and a member of the American Pediatric Society and the Society for Pediatric Research. From 1951 to 1961 he was a member of the editorial board of the American Journal of Diseases of Children. In 1951 Pope Pius XII conferred upon him the order of Knight of St. Gregory the Great.

CO-GEL

THE NEW ANTACID



Holbert, J. M., Noble, N., and Grote, I. W.—Jnl. Amer. Pharm. Assoc. (Sci. Ed.) 37,292 (1948).

Now, an antacid tablet with the effectiveness of a liquid!

CO-GEL is not just another antacid, but rather it's an entirely *new antacid compound* for gastritis, hyperacidity and peptic ulcers. It is an Aluminum Hydroxide formulation with Magnesium Carbonate Co-Precipitate. The Co-Precipitate, a new chemical, gives CO-GEL Tablets the speed of action and the duration of a liquid antacid.

The above chart compares the antacid action of the COGEL Tablet formula with both liquid and dry $Al(OH)_3$. Notice that CO-GEL neutralizes acid faster than $Al(OH)_3$ dried gel tablets and has a prolonged buffering action. The CO-GEL curve parallels that of liquid $Al(OH)_3$.

Liquid CO-GEL, containing the Co-Precipitate, is also available. CO-GEL is reasonably priced to the patient. Availability: CO-GEL Tablets (bottles of 100 and 1,000) CO-GEL Liquid (pints and gallons).

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write to Dept JL-100

FORMULA

Each CO-GEL Tablet, and teaspoonful of CO-GEL Liquid, contains 330 mg. of Aluminum Hydroxide Magnesium Carbonate Co-Precipitate. Tablets have a chewable base. Both forms are mint flavored.

CONTRAINDICATIONS

None.

DOSAGE

For relief of hyperacidity, peptic ulcers or gastritis, chew one tablet (or take one teaspoonful). Repeat in 1 hr. if necessary.

ULMER

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COMPANY**

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Special cough formula for children

Pediacof®

Each teaspoon (5 ml.) contains codeine phosphate 5 mg.,
Neo-Synephrine® hydrochloride (brand of phenylephrine hydrochloride) 2.5 mg.,
chlorpheniramine maleate 0.75 mg. and potassium iodide 75 mg.

soothing decongestant and expectorant

relieves cough
nasal drip
congestion
running nose
sneezing
eases expectoration

bright red, pleasant-tasting, raspberry-flavored syrup

Pediacof is different. It is designed especially for children, and each ingredient is in the right proportion. The potassium iodide in Pediacof is so well masked that it is virtually unnoticeable. Children like the sweet raspberry flavor of bright red Pediacof.

Dosage: Children from 6 months to 1 year, ¼ teaspoon; from 1 to 3 years, ½ to 1 teaspoon; from 3 to 6 years, 1 to 2 teaspoons; and from 6 to 12 years, 2 teaspoons. These doses are to be given every four to six hours as needed.

How supplied: Bottles of 16 fl. oz.

Available on prescription only.
Exempt Narcotic.

Side effects: The only significant untoward effects that have occurred are mild anorexia and an occasional tendency to constipation. However, discontinuance of Pediacof has seldom been required. Mild drowsiness occurs in some patients but, when cough is relieved, the quieting effect of Pediacof is considered beneficial in many instances.

Precautions and contraindications: Patients with tuberculosis or those who are known to be sensitive to iodides should not be given Pediacof.

Caution should be exercised if Pediacof is administered to patients with cardiac disorders, hypertension or hyperthyroidism.

Warning: May be habit forming.

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The Journal-Lancet

97th Year of Publication

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SERVES THE MEDICAL PROFESSION OF THE UPPER MIDWEST

APRIL 1966

Rowell responds to the 'cold' patient's comprehensive problem with the 'total therapy' concept

Colrex Compound

PHENYLEPHRINE TO RELIEVE NASAL CONGESTION with a potent vaso-constrictor that does not lead to "rebound congestion."

CHLORPHENIRAMINE TO COMBAT EXCESSIVE SECRETION without causing excessive drying of the delicate nasal mucosa.

CODEINE TO SUBDUE COUGH remains the best antitussive and appears to act synergistically with PAPAVERINE in the relief of cold symptoms—and to enhance aspirin analgesia.

ALUMINUM ASPIRIN TO REDUCE FEVER AND ACHE with less possibility of salicylate-induced gastric upset. PLUS VITAMIN C TO HELP MAINTAIN CAPILLARY INTEGRITY.

NEGLECTS NO ASPECT OF THE RESPIRATORY SYNDROME

Colrex Compound

EACH CAPSULE CONTAINS:

Codeine phosphate (Warning: May be habit-forming)	16 mg.
Papaverine hydrochloride	16 mg.
Aluminum aspirin	300 mg.
Phenylephrine hydrochloride	5 mg.
Chlorpheniramine maleate	2 mg.
Vitamin C	100 mg.

Dosage: Adults, 1 capsule 3 or 4 times daily; children, according to age and weight.

Indications: Cough, congestion, headache, discomfort and muscular aches and pains in coryza, rhinitis, sinusitis, pharyngitis, laryngitis, tracheitis, bronchitis, grippe, influenza and pneumonia.

Side effects and precautions: Side effects are infrequently encountered. Codeine and aluminum aspirin should not be given to patients with known idiosyncrasies to these drugs. Antihistaminic agents may cause drowsiness in susceptible individuals. Colrex Compound should be used with caution in hypertensive patients.

Caution: Federal law prohibits dispensing without a prescription. Class B narcotic.

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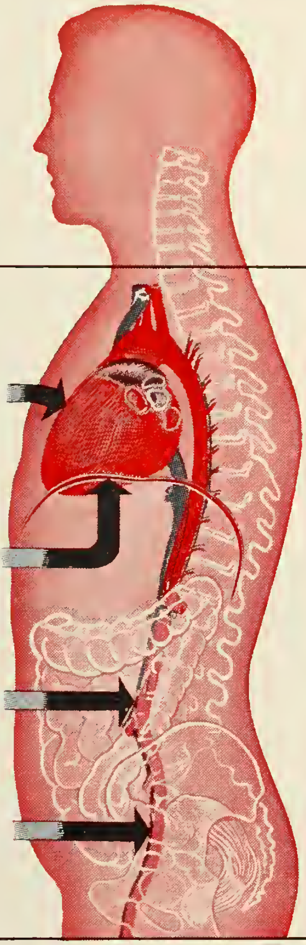
In Cardiovascular Patients–

Increased intrathoracic and intra-abdominal pressure from straining



Metamucil

. . . to prevent straining at stool and its adverse effect on blood pressure, cardiac output and pulmonary circulation.

Average Adult Dosage:

One rounded teaspoonful of Metamucil (or one packet of Instant Mix Metamucil) in a glass of cool liquid one to three times daily.

METAMUCIL®

brand of psyllium hydrophilic mucilloid

Metamucil Powder: 4, 8 and 16-ounce containers. Instant Mix Metamucil: cartons of 16 and 30 single-dose packets.

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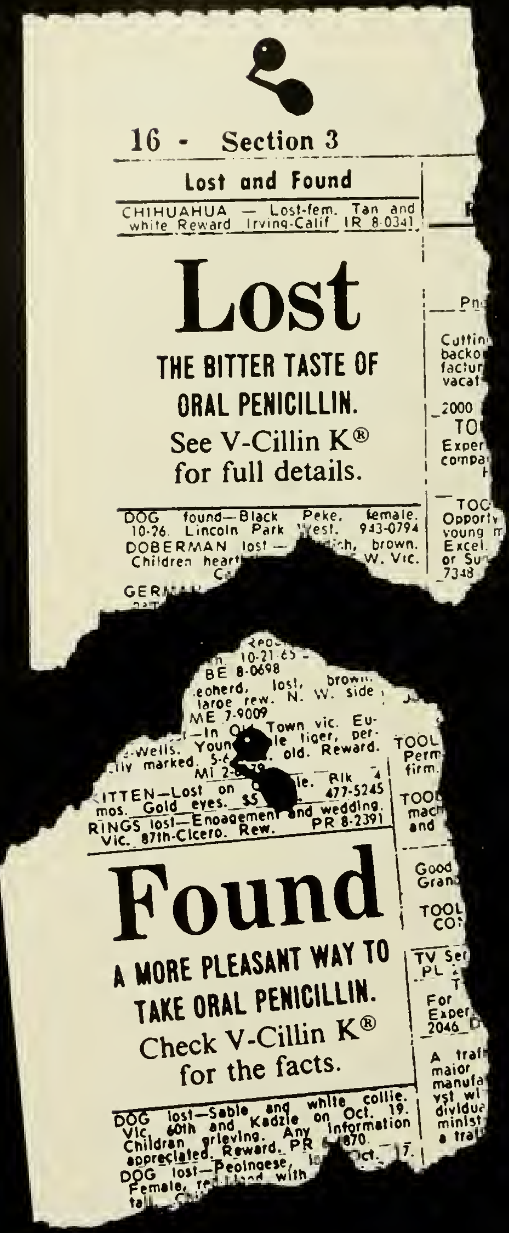

16 - Section 3

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Lost

THE BITTER TASTE OF ORAL PENICILLIN.

See V-Cillin K®
for full details.

DOG found—Black Peke, female. 10-26. Lincoln Park West. 943-0794

DOBERMAN lost — ...ch, brown. Children heart... W. Vic.

BE 8-0698

KITTEN—Lost on ... mos. Gold eyes. $5 ... 477-5245

RINGS lost—Engagement and wedding. Vic. 87th-Cicero. Rew. PR 8-2391

Found

A MORE PLEASANT WAY TO TAKE ORAL PENICILLIN.

Check V-Cillin K®
for the facts.

DOG lost—Sable and white collie. Vic. 60th and Kedzie on Oct. 19. Children grieving. Any information appreciated. Reward. PR ...870.

Patients won't complain about bitter penicillin taste when you specify V-Cillin K. Here's why: It has a special coating, only one and a half *thousandths* of an inch thick. Because it is designed to dissolve after approximately six seconds, this barrier to bitterness remains on the tablet as it slides past the tongue. When the tablet reaches the stomach, however, the coating has dissolved, and the penicillin is ready for immediate absorption into the bloodstream.

Result? The proved efficacy of potassium penicillin V without the penalty of bitter taste.

Indications: V-Cillin K is an antibiotic useful in the treatment of streptococcus, pneumococcus, and gonococcus infections and infections caused by sensitive strains of staphylococci.

Contraindications and Precautions: Although sensitivity reactions are much less common after oral than after parenteral administration, V-Cillin K should not be administered to patients with a history of allergy to penicillin. As with any antibiotic, observation for overgrowth of nonsusceptible organisms during treatment is important.

Usual Dosage Range: 125 mg. (200,000 units) three times a day to 250 mg. every four hours.

Supplied: Tablets V-Cillin K, 125 or 250 mg., and V-Cillin K, Pediatric, 125 mg. per 5-cc. teaspoonful, in 40, 80, and 150-cc.-size packages.

Lilly

V-Cillin K®
Potassium Phenoxymethyl Penicillin

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available to physicians
upon request.
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The Journal-Lancet

Volume 86, No. 4, April 1966

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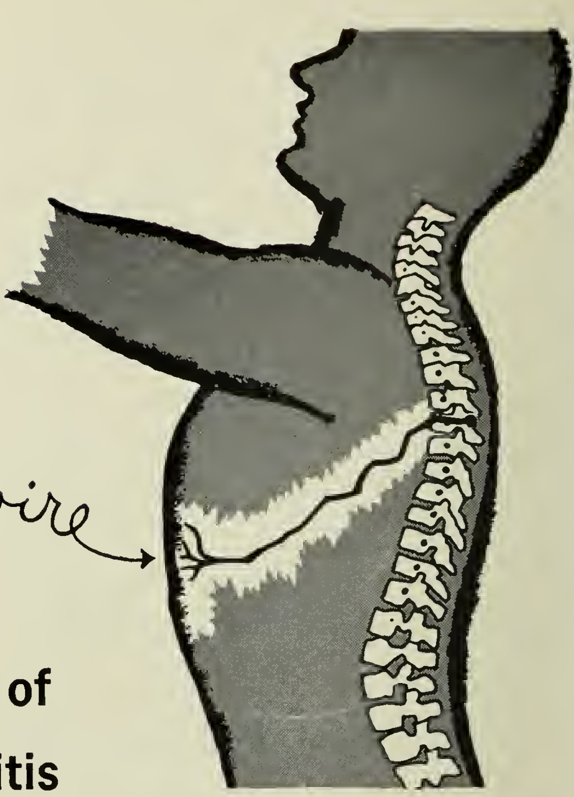

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the Searing *Pain* of Inflammatory Neuritis

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provides the *selective* fast-acting relief . . .

Repeatedly in published clinical studies,[1-10] investigators stress the following therapeutic characteristics:

- relief of inflammatory pain (non-traumatic) is prompt—particularly when administered early.[1-4]
- disability time is shortened from weeks to days.[7]
- so specifically effective is Protamide that a positive response is diagnostic of inflammatory neuritis.[3,4]
- prompt relief is observed even in ophthalmic herpes zoster.[5,6]
- incidence of sequelae such as postherpetic neuralgia is reduced.[1-4]
- consistently described as the therapy of choice.[1,3-6]

Administration:

In neuritis and herpes zoster, one ampul I.M. daily for 2 to 5 days usually relieves pain completely in patients treated early. Well tolerated.[1-10] However, inadvertent intravenous administration may cause anaphylactoid reaction.

—Boxes of 10 ampuls, 1.3 cc. each.—

References: (1) Baker, A. G.: Penn. Med. J. *63*:697-698 (May) 1960. (2) Smith, R. T.: New York Med. *8*:16-19 (Aug. 20) 1952. (3) Smith, R. T.: Med. Clin. N. America (March) 1957. (4) Lehrer, H. W.; Lehrer, H. G., and Lehrer, D. R.: Northw. Med. *54*:1249-1252 (Nov.) 1955. (5) Sforzolini, G. S.: Arch Ophthal. 62-381-385 (Sept.) 1959. (6) Shupala, E.: W. Virginia Med. J. *56*:191-193 (June) 1960. (7) Xander, G. W.: Western Med. *1*:14-17 (Sept.) 1960. (8) Combs, F. C., and Canizares, O.: New York J. Med. (Mar. 15) 1952, pp. 706-708. (9) Marsh, W. C.: U.S. Armed Forces Med. J. *1*:1045 (Sept.) 1950. (10) Love, T. R.: Rocky Mountain Med. J. *50*:873 (Nov.) 1953.

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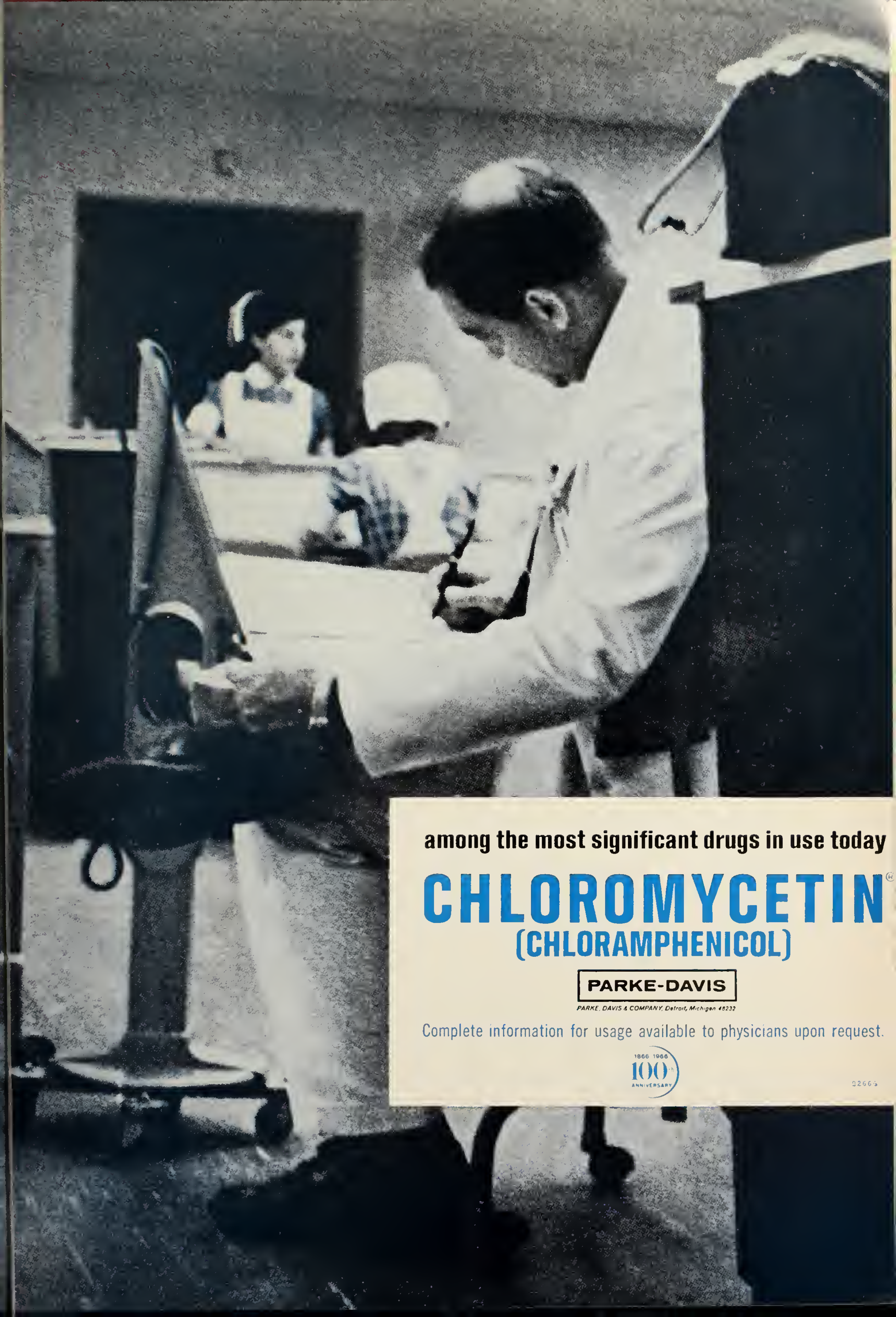

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(meprobamate)

Indications: 'Miltown' (meprobamate) is effective in relief of anxiety and tension states. Also as adjunctive therapy when anxiety may be a causative or otherwise disturbing factor. Although not a hypnotic, 'Miltown' fosters normal sleep through both its anti-anxiety and muscle-relaxant properties.

Contraindications: Previous allergic or idiosyncratic reactions to meprobamate or meprobamate-containing drugs.

Precautions: Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Usual adult dosage: One or two 400 mg. tablets three times daily. Doses above 2400 mg. daily are not recommended.

Supplied: In two strengths: 400 mg. scored tablets and 200 mg. coated tablets.

Before prescribing, consult package circular.

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Complications of Antibiotic Therapy in the Management of Bacterial Infections

WILLIAM J. MARTIN, M.D.
Rochester

Only by continuous reevaluation can one assess the comparative advantages of new antibacterial agents and the continued value of older agents. Such a procedure is essential, especially since the benefits, as well as the undesirable effects, of an antibacterial agent may not become known until several years have elapsed after its clinical availability. The purpose of this report is to outline some of the undesirable effects which may complicate the antibiotic therapy of bacterial infections. Consideration will be limited to the complications of antibiotics now commercially available.

THE PENICILLINS

Of the naturally occurring penicillins, penicillin G, penicillin O, and penicillin V are produced commercially. More recently, a series of semisynthetic penicillins, for example, phenethicillin (Syncillin®, Darcil®), ampicillin (Polycillin®, Penbritin®), methicillin (Staphcillin®, Dimocillin-RT®), nafcillin (Unipen®), oxacillin (Prostaphlin®, Resistopen®), and cloxacillin (Tepogen®) has been marketed.[1]

Penicillin O is no longer in common use since it has become apparent that it is cross-allergenic with penicillin G. On oral administration, penicillin V and phenethicillin are considered interchangeable for clinical use; phenethicillin may give higher serum levels, but this difference does not appear significant since, weight for weight, the drugs have a similar antibacterial effect when evaluated by so-called serum bactericidal tests. Ampicillin, which is effective against some gram-negative bacilli, including strains of Escherichia coli, Proteus mirabilis, Haemophilus influenzae, and Salmonella and Shigella organisms, is destroyed by penicillinase and, hence, is not effective against penicillin G–resistant staphylococci. Methicillin, nafcillin, oxacillin, and cloxacillin resist the action of penicillinase and hence are effective against penicillin G–resistant staphylococci; of these drugs, only methicillin is not absorbed on oral administration.

Allergy is the chief difficulty encountered with the use of the penicillins. Cross-allergenicity among the natural penicillins and the semisynthetic penicillins apparently is reflective of the fact that they share the 6-aminopenicillanic acid (6-APA) nucleus.

Various skin reactions, glossitis, stomatitis, drug fever, serum sickness, and anaphylaxis may complicate the use of the penicillins. More unusual complications include purpura, pericarditis, toxic psychoses, and hematemesis due to an urticaria-like reaction of the gastric mucosa. Diffuse vasculitis may be a rare manifestation of penicillin hypersensitivity. Gastrointestinal irritation, including diarrhea, may follow the use of an orally administered penicillin, but it is seldom severe enough to require discontinuation of therapy. Pain or intramuscular injection is more likely on use of benzathine penicillin G, ampicillin, and nafcillin.

For the last few years, use of the potassium

WILLIAM J. MARTIN *is with the Section of Medicine, Mayo Clinic and Mayo Foundation, Rochester.*

salt in the manufacture of aqueous crystalline penicillin G has been the usual practice. In patients whose intake of sodium should be restricted, this represents a contribution; but in some patients, such as those having renal dysfunction and receiving penicillin therapy, the increased intake of potassium must be considered. Especially in patients with decreased renal function, large doses of potassium penicillin G given intravenously may result in cardiac arrest. Each 15,000,000 units of aqueous crystalline penicillin G supplies 975 mg. (25 mEq.) of ionic potassium. Similar considerations are required on use of the semisynthetic penicillins. For example, in the management of patients having heart failure or renal dysfunction, one should recall that each 4 gm. of methicillin supplies 230 mg. (10 mEq.) of ionic sodium.

Penicillin G, especially when given in large amounts for prolonged periods, rarely has caused anemia, evidently reflecting immune erythrocyte destruction.[2] Granulopenia and anemia have occurred after administration of methicillin. Oxacillin has caused transient leukopenia. Some of the penicillins have been accused of other forms of hematotoxicity on occasion, but these contentions are more difficultly established.

Penicillin G, when given in large amounts, may cause cortical irritation including convulsions. Such complications are most likely to occur in patients with decreased renal function. Since the drug has caused acute psychosis and convulsions and some victims of an anaphylactoid reaction have had chronic brain damage, perhaps one should be more aware of its potential neurotoxicity.

Whether methicillin has nephrotoxic effects is uncertain at this writing.

During therapy with ampicillin, oxacillin, and cloxacillin, the serum glutamic oxalacetic transaminase (SGOT) activity may be increased, but the exact significance of this is not clear.

Phenethicillin, oxacillin, cloxacillin, and nafcillin are not well absorbed after oral administration unless the stomach is otherwise empty. Food interferes with the absorption of these drugs, and consequently, the decreased levels in serum may be insufficient to eradicate an infection. Although penicillin V and phenethicillin are said to be interchangeable for clinical use, the potassium salt of penicillin V has the advantage that its absorption is not similarly reduced.

Use of the penicillins may depress the coccal members of the body flora and encourage the development of bacteremia, urinary infection, pneumonia, and other infections caused by overgrowth of resistant organisms such as gram-negative bacilli and Candida. Periodic examination of the sputum and stools may allow detection of changes in the body flora in time to avert clinical superinfection. Occasionally, in series of patients treated with methicillin, as many as a third have experienced superinfections due to gram-negative bacilli; fatal bacteremia due to gram-negative bacilli has occurred.

Strains of Staphylococcus aureus isolated from clinical material in British hospitals have demonstrated an increasing incidence of resistance to methicillin.[1] These strains may show a corresponding increase in resistance to other penicillinase-resistant semisynthetic penicillins. The presumption is that when these drugs have been employed in a given environment for a period of time, strains of staphylococci will demonstrate increasing resistance to their action, as has occurred in Britain. This ominous possibility should be sufficient to militate against indiscriminate use of these drugs.

STREPTOMYCIN AND ALLIED DRUGS

This heading encompasses streptomycin, dihydrostreptomycin, neomycin sulfate (Mycifradin®), kanamycin sulfate (Kantrex®), and paromomycin (Humatin®). Dihydrostreptomycin is no longer in common use because of its potential toxicity, neomycin has been largely replaced by kanamycin for parenteral administration, and paromomycin is given only by the oral route.

Streptomycin and dihydrostreptomycin. Streptomycin is less likely to produce hearing loss than is dihydrostreptomycin or a combination of the two substances. Dihydrostreptomycin has produced deafness even after use of the drug has been stopped. It is recommended currently that dihydrostreptomycin only be used when the patient needs such an agent and can accept dihydrostreptomycin but not streptomycin. Although streptomycin may damage vestibular function of the eighth cranial nerve, this is not so calamitous as deafness, and the dysequilibrium may be compensated, at least partly, by ocular mechanisms. The incidence of ototoxicity usually is proportional to the daily dose and duration of streptomycin therapy. The likelihood of ototoxicity is greater in infants, the aged, patients who are dehydrated, and those with impaired renal function. Ototoxic residua have occurred in children born to mothers receiving streptomycin. As a generalization, in normal adults, ototoxicity is unlikely if 2 gm. or less of streptomycin is given daily for no longer than fourteen days, or 1 gm. is administered daily for four weeks or less. The concentration of streptomycin in blood should not exceed 25 μg. per milliliter, and the daily dose should be adjusted accordingly. A 0.25- to 0.5-gm. dose of streptomycin, given every two to four days, may suffice in the azotemic patient.

It is not definitely known if prior use of streptomycin or other ototoxic drugs like kanamycin or vancomycin increases the change of ototoxicity on future use of streptomycin, but this possibility should be considered when the drug is administered. In any event, ototoxic drugs should not be used concurrently.

Streptomycin, dihydrostreptomycin, neomycin, kanamycin, polymyxin B, and colistin share a potential curariform action that may produce neuromuscular block and respiratory arrest, especially on intracavitary instillation. Such an effect would be unusual when streptomycin is given intramuscularly, but the possibility is considered in infants, the aged, patients with renal disease or hypoxic states, and those receiving certain drugs such as muscle relaxants, sedatives, narcotics, and anesthetic agents. In patients having such an untoward reaction, use of neostigmine or calcium may be helpful. The previously mentioned antibiotics are contraindicated in patients who may have myasthenia gravis.

Optic neuritis may follow the administration of either streptomycin or chloramphenicol and is a theoretic reason for avoiding concurrent use of these drugs. Ancillary data suggest that these drugs may induce the complication via the mechanism of pyridoxine deficiency.

Pericarditis is a rare complication of therapy with streptomycin and also has occurred after the use of either a penicillin or a tetracycline.

Rashes, fever, paresthesias, headache, and albuminuria also may result from the use of streptomycin.

It is to be emphasized that streptomycin and dihydrostreptomycin are not cross-allergenic.

Neomycin. Intramuscular use of neomycin has decreased, especially since the advent of kanamycin. Bacterial resistance to neomycin has increased in recent years, perhaps because neomycin is incorporated in procedures used to prepare the colon before operation and also because the drug is a constituent of numerous preparations for local use, such as sprays and creams. In this regard, there is bacterial cross resistance among neomycin, kanamycin, and paromomycin, and partial cross resistance among these drugs and streptomycin. Therefore, incautious use of any one of these drugs may decrease the future applicability of the others. Because of its potential nephrotoxicity and neurotoxicity when given systemically, neomycin is reserved principally for [1] topical application and [2] oral administration. Via the oral route, neomycin is used in preoperative preparation of the colon, in certain cases of hepatic coma, and alone or with polymyxin B in cases of enteric salmonellosis and shigellosis.

Since neomycin is not absorbed well from the intestine, as much as 8 to 12 gm. have been given daily by the oral route in certain patients, such as those with hepatic coma. Preferably, no more than 4 gm. orally per day should be given, especially in patients with ulcerative bowel disease, hepatic insufficiency, or renal disease, because blood concentrations may become sufficiently high as to induce toxic effects. If neomycin is given intramuscularly, a daily dose of 1 gm. should not be exceeded.

Neomycin-induced ototoxicity principally involves auditory function and is irreversible. It has occurred after the drug has been used orally, intramuscularly, as an aerosol, on intracavitary instillation, and after topical application to cutaneous burns.

In addition to neomycin, there are five drugs that can cause paresthesias, usually circumoral and of the acral parts. These same drugs are the ones capable of a curariform effect and are streptomycin, dihydrostreptomycin, kanamycin, polymyxin B, and colistin.

Malabsorptive effects on oral use of neomycin may resemble those of nontropical sprue and include steatorrhea, azotorrhea, and interference with the absorption of vitamins, sugars, and minerals, as well as small-bowel alterations on biopsy. Since these malabsorptive effects are produced by doses commonly used to suppress the fecal flora, as in certain patients having hepatic coma, it is wise to consider them in the management of an individual case. Neomycin-induced malabsorption may be the basis for the hypocholesterolemic effect that may occur after the drug is used orally.

Administration of neomycin may produce skin reactions, including contact dermatitis, from its local use. Neomycin also has caused so-called drug fever.

Neomycin, streptomycin, the tetracyclines, and other drugs may depress the gram-negative elements of the normal flora and allow overgrowth of resistant staphylococci. Bacteremia, pneumonia, and other staphylococcal superinfections may occur in addition to staphylococcal enterocolitis. Candidiasis also may complicate neomycin therapy.

Kanamycin. As aforementioned, organisms show almost complete cross resistance to neomycin, kanamycin, and paromomycin as well as one-way cross resistance to streptomycin and kanamycin or the kindred drugs; that is, organisms resistant to kanamycin are resistant to streptomycin, but organisms resistant to streptomycin may be sensitive to kanamycin. Incautious use of these allied drugs may decrease the clinical applicability of kanamycin.

Because of kanamycin's potential toxicity, the daily intramuscular dose for an adult of average weight is 1 gm. and should not exceed 1.5 gm. even for heavier patients. One should be hesitant to continue therapy beyond fourteen days because of the drug's capacity to cause deafness (which may be delayed in onset and is irreversible). Like neomycin, kanamycin is not absorbed well from the intestine, but one should avoid giving more than 4 gm. per day by the oral route. Other untoward effects include rashes, fever, headache, nephrotoxicity, curariform action, paresthesias, and superinfection. As with neomycin, malabsorptive effects may occur after oral use of kanamycin.

In addition to kanamycin, there are at least four other potentially ototoxic drugs: streptomycin, dihydrostreptomycin, neomycin, and vancomycin. Whether ristocetin or colistin is ototoxic is uncertain. One should avoid concurrent and, perhaps, sequential use of these ototoxic drugs.

Paromomycin. This agent is used orally in certain cases of enteric salmonellosis, shigellosis, and amebiasis and to suppress the intestinal flora before operation as well as in patients with hepatic coma. In order to prevent neurologic complications that may reflect inadequate hepatic filtration and consequent systemic absorption of ammonia due to the action of intestinal bacteria on dietary protein in the patients with hepatic coma, the three drugs most commonly used are neomycin, kanamycin, and paromomycin. Paromomycin is not well absorbed after oral administration and is ineffective in systemic infections. Paromomycin is given orally in 500-mg. doses four to six times daily; an initial dose of 4 gm. has been recommended. Excessive oral dosage is avoided since the agent is potentially nephrotoxic.

Untoward effects include dermatitis, headache, candidal superinfection, vomiting, and diarrhea. Loose stools after the drug is used may be confused with an underlying disease.

THE TETRACYCLINES

The commercially available members of this group of drugs are chlortetracycline hydrochloride (Aureomycin®), oxytetracycline hydrochloride (Terramycin®), tetracycline (Achromycin,® Tetracyn®, Panmycin KM®, Polycycline®), demethylchlortetracycline (Declomycin®), and rolitetracycline (Syntretin®, Velacycline®).

As a generalization, chlortetracycline, oxytetracycline, and tetracycline are considered to be interchangeable for clinical use. Demethylchlortetracycline has been said to produce higher and more sustained serum levels but this is disputed. Rolitetracycline is given parenterally and is said to give higher serum levels and to be followed by less pain on intramuscular injection than other available preparations.

Nausea, vomiting, and looseness of the stools may occur on oral use of these drugs. However, when frank diarrhea results, smear and culture of the stool should be carried out in order to exclude staphylococcal enterocolitis. Superinfection may be due to organisms, other than staphylococci, such as Candida, Proteus, and Pseudomonas and result in other types of infection such as pneumonia, bacteremia, and so forth.

Drug fever, rashes, glossitis, stomatitis, metallic taste in the mouth, decreased sense of smell, and pruritus ani et vulvae are other untoward effects. Anaphylaxis, acute transitory myopia, hematotoxicity (thrombocytopenia), and pericarditis are rare complications. Chemical phlebitis at the site of injection is frequent after intravenous administration.

When a tetracycline is added to solutions employed in peritoneal dialysis, the possibility of an untoward effect of the antibiotic should be considered. In markedly azotemic patients, levels in serum may approach the therapeutic range within fifteen to twenty hours.

The tetracyclines are not detectable in most normal tissues twelve to twenty-four hours after their administration is discontinued, but they may be retained indefinitely in mineralized tissues. Pigmentation and faulty enamel formation of children's teeth may follow use of the drugs either by the mother in late pregnancy or by the child in early life. Initially, the pigmentation is bright yellow but turns brownish with increasing age; exposure to light may intensify the pigmentation.

The tetracyclines also are retained in bone apparently because of chelating properties of these agents and formation of a tetracycline-calcium-orthophosphate complex. The question has been raised whether deposition of the drugs in bones might inhibit their linear growth in premature infants, as has occurred in experimental animals.

After prolonged tetracycline therapy, fluorescence of the nails may be demonstrable, and rarely, discoloration and onycholysis can be seen by the naked eye.

The tetracyclines produce antianabolic effects that may have clinical significance in patients having reduced renal function. Negative nitrogen balance, increased urinary loss of such substances as sodium and riboflavin, increased azotemia, hyperphosphatemia, acidosis, and loss of weight may occur. The antianabolic effects of the tetracyclines, which apparently reflect inhibition of incorporation of amino acid into protein, do not appear to have great significance in patients with adequate renal function, although the manifestations in them are detectable by metabolic studies.

Fatal liver disease may occur in persons given excessive amounts of a tetracycline. Pregnancy, underlying hepatic disease, conjoint use of other hepatotoxic drugs, and impaired renal function increase the chances of hepatotoxicity. The possibility of this complication is enhanced when more than 2 gm. per day have been given intravenously, but the duration of therapy as well as the daily dose should be minimized, when the drugs are given by any route. Jaundice, azotemia, acidosis, gastrointestinal bleeding, and hypotension may precede death. In doubtful cases, the serum concentration of the drug should be maintained at less than 15 μg. per milliliter.

Photosensitivity, manifested by marked erythema and sometimes edema, is associated more often with demethylchlortetracycline therapy but has occurred after chlortetracycline, oxytetracycline, or tetracycline has been used.

A tetracycline, especially when administered intravenously, may interfere with blood coagulation; increased clotting time, decreased plasma prothrombin activity, lowered prothrombin consumption, and retarded thromboplastin generation have been described.[1]

A reversible Fanconi syndrome can result from ingestion of outdated or degraded tetracycline. Unexplained vomiting, dehydration, muscle weakness, polydipsia, polyuria, glycosuria with a normal blood sugar, or metabolic acidosis may manifest the reaction; proteinuria, acetonuria, aminoaciduria, Bence-Jones proteinuria, potassium depletion, and loss of calcium and phosphate also occur. Lethargy may progress to coma. Gait disturbances may last several months. Aminoaciduria may persist after other alterations disappear. Packaging of the tetracyclines with alpha-lactose monohydrate may delay degradation of the drugs. A degradation product of tetracycline such as epianhydrotetracycline or anhydrotetracycline is suspected as causing the inhibition of tubular reabsorption.

An isolated defect of renal tubular function, manifested by polyuria and hyposthenuria, after ingestion of demethylchlortetracycline has been described.[3] This example of so-called nephrogenic diabetes insipidus appears to be a reversible effect of the intact drug and unrelated to excessive dosage.

With full therapeutic doses of a tetracycline in infants, increased intracranial pressure with bulging fontanels has been observed but has disappeared on cessation of treatment.

CHLORAMPHENICOL

Aplastic anemia, thrombocytopenia, and granulocytopenia have occurred after both short-term and prolonged therapy with chloramphenicol (Chloromycetin®) but rarely have complicated its local use, as may happen with use of ocular solutions. Regular studies to detect eosinophilia, leukopenia, thrombocytopenia, anemia, reticulocytopenia, and rising serum levels of iron should be carried out. Hematotoxicity may represent an accentuated normal response to the drug since mild reversible changes are not rare, and large doses given for prolonged periods will cause maturation arrest in a majority of subjects. However, in certain individuals, hypersensitivity probably contributes partially to the drug's hematotoxicity. Hematotoxicity is more frequent in Caucasian girls less than 12 years old. Some recent work[4] indicates that 100 mg. of L-phenylalanine per kilogram of body weight per day given orally may ameliorate the hematotoxicity. Other hematotoxic drugs include ristocetin, and, less frequently, streptomycin, the tetracyclines, and novobiocin. Penicillin G, especially when given in large amounts for prolonged periods, rarely has caused anemia, evidently reflecting immune erythrocytic destruction.[2] Anemia also has occurred after the administration of methicillin. Novobiocin, methicillin, oxacillin, colistin, cephalothin, and lincomycin have caused transient leukopenia. Actually, all antibacterial agents have been accused of hematotoxicity on occasion, but contentions against the others are difficultly established.

The fatal "gray syndrome" may occur in infants given chloramphenicol. Anorexia, abdominal distension, lethargy, flaccidity, hypothermia, respiratory distress, and "gray cyanosis" may reflect excessive concentration of the drug because of deficiencies of drug conjugation and excretion due to immature enzyme systems in the infant.

A "typhoid shock" syndrome occurs after the drug is used in typhoid fever, and the shock, presumably caused by excessive release of endotoxin, resembles so-called bacteremic shock due to other gram-negative bacilli.

As aforementioned, chloramphenicol and streptomycin may cause optic neuritis. The mechanism of the neuropathy may concern drug-induced pyridoxine deficiency.

Other untoward effects include stomatitis, glossitis, candidal superinfection, rashes, fever, and, on oral use, gastrointestinal irritation.

POLYMYXIN B AND COLISTIN

Polymyxin B. Untoward effects of polymyxin B (Aerosporin®) include nephrotoxicity, pain on intramuscular injection, fever, flushing, pruritus, rashes, superinfection, paresthesias, cerebellar ataxia, headache, and a curare-like effect.

Colistin. This drug differs from polymyxin B in only one of its amino acids and in the configuration of the molecule; some workers believe that the term "colistin" should be discarded in favor of polymyxin E. Colistin sulfate is used orally whereas sodium colistimethate (Coly-Mycin®) is the form used parenterally. The antibacterial spectra of polymyxin B and colistin are identical, and there is bacterial cross resistance to the two drugs.

Colistin initially was described as being less toxic than polymyxin B, but more recently this has been disputed.[1] When amounts of colistin are given to produce an antibacterial effect similar to that obtained with recommended doses of polymyxin B, the untoward effects of the two drugs may be similar and of equal incidence. In addition, transient leukopenia, auditory disturbances, and hepatotoxicity have been described as complicating use of colistin. A lesser amount of pain on intramuscular injection of colistin reflects its being marketed in combination with a local anesthetic; employing a 1 to 2% solution of an anesthetic in making dilutions of polymyxin B provides a similar effect.

ERYTHROMYCIN AND ALLIED DRUGS

Erythromycin. The parent drug was introduced in 1952 and erythromycin propionate in 1958. The lauryl sulfate salt of erythromycin propionate has been named erythromycin estolate. Erythromycin estolate is the most active form of erythromycin; it provides faster, higher, and more persistent concentration in serum than the erythromycin base, even when taken with food. Unfortunately, erythromycin estolate has proved to be potentially hepatotoxic.

Hepatic dysfunction has appeared in some patients after a few days of treatment with erythromycin estolate but generally it has occurred after one or two weeks of continuous therapy or after several courses of the drug. Jaundice, abnormal results of liver function tests, and eosinophilia may occur, but the findings usually subside rapidly when use of the drug is stopped. Symptoms reappear promptly if the drug is readministered, usually within forty-eight hours. Erythromycin, which is not hepatotoxic in its basic form, probably acquires this capacity by esterification of a side chain, that is, when a simple hydroxyl group is replaced by the propionyl radical. The effect seems to be one of intrahepatic cholestasis resulting from a form of sensitization. Because of the hepatotoxicity of erythromycin estolate, use of another salt or the erythromycin base is preferable unless circumstances in the individual case are extraordinary.

Mild gastrointestinal irritation may occur after the agent is used orally, but there is little evidence of serious allergic reactions to erythromycin base. Dermal reactions are unusual and anaphylaxis is extremely uncommon.

Triacetyloleandomycin. This agent is a chemical derivative of the antibiotic oleandomycin that has been prepared by the acetylation of three hydroxyl groups in the parent molecule. After oral administration, more rapidly attained and higher blood concentrations result than after oral administration of a comparable amount of the parent agent. The scope of the therapeutic effectiveness of triacetyloleandomycin (Cyclamycin®, TAO®) parallels that of erythromycin. In cases of mild and moderately severe staphylococcal infections caused by erythromycin-resistant strains, triacetyloleandomycin may have application, since there is a chance of approximately 70% that the organisms may be sensitive to triacetyloleandomycin.

Side effects of triacetyloleandomycin include skin reactions, fever, anorexia, nausea, and an increased number of stools. Reactions of the anaphylactoid type have occurred on rare occasions. Superinfection with nonsusceptible organisms is worthy of at least theoretic consideration. Triacetyloleandomycin, like propionyl erythromycin ester and erythromycin estolate, is hepatotoxic. The derivatives of oleandomycin and erythromycin apparently acquire this capacity by esterification of their side chains. The side chain esterified in both antibiotics is similar; and, as previously discussed in the case of the erythromycin derivatives, when a hydroxyl group is replaced, as by the acetyl radical in the case of oleandomycin, the agent becomes hepatotoxic. Whereas erythromycin base may be an adequate substitute for its chemical derivatives in most of the infections requiring use of such a drug, oleandomycin is not sufficiently effective to replace triacetyloleandomycin.

Because alterations in liver function have occurred in some patients after two weeks or more of therapy with triacetyloleandomycin, its routine use is not recommended in the management of infectious diseases that may require more than ten days of continuous therapy. If therapy is to be continued beyond ten days, tests of liver function should be carried out. Evidence of hepatic dysfunction appears to be reversible shortly after use of the drug is discontinued.

In addition to the propionyl ester of erythromycin and triacetyloleandomycin, the tetracyclines, especially when given intravenously in excessive dosage, are potentially hepatotoxic, and their use may result in jaundice. An exogenous substance causing pigmentation similar to jaundice may follow administration of novobiocin and more often is the basis for discoloration than is hyperbilirubinemia following use of that drug. Colistin, lincomycin, and cephalothin may be hepatotoxic, but data in this regard are not definitive.

Novobiocin. This agent is about as effective as erythromycin against staphylococci. Whereas novobiocin (Albamycin®) is effective against certain other organisms, its use is virtually restricted to selected infections due to staphylococci or P. mirabilis that resist other agents. It has been used in infections due to other organisms such as hemolytic streptococci and pneumococci in persons allergic to penicillin.

The relatively high incidence of allergic dermatitis militates against the more common use of novobiocin. Cutaneous lesions of a hemorrhagic nature may indicate that novobiocin has a coumarin-like effect. Other toxic reactions that occur after its use include drug fever, yellowing of the sclera, and, after oral administration, slight abdominal cramping, nausea, and increased number of stools. Transient leukopenia occurs and, rarely, anemia, agranulocytosis, and thrombocytopenia have been reported.[1] In most adults, the scleral discoloration following use of novobiocin reflects the transient deposition of a harmless pigment produced in the metabolism of novobiocin rather than bile pigment. The yellow pigment also has been found in the plasma of patients receiving the drug, and its presence may interfere with determination of serum bilirubin and the icteric index. In young children, novobiocin may interfere with the conjugation of bilirubin, and rarely in adults the drug may have caused hyperbilirubinemia and impaired sulfobromophthalein excretion. When icteral discoloration appears during therapy, administration of the drug should be discontinued until the nature of the pigment can be ascertained. Pigmentation resulting from the metabolite of novobiocin, as distinguished from that of true jaundice, does not contraindicate continued use of the drug.

Use of novobiocin, erythromycin, and other antibacterial agents, which like penicillin may depress the coccal members of the body flora, may thereby encourage the production of bacteremia, urinary infection, pneumonia, and the like by gram-negative bacilli. When such organisms are relieved of their natural ecologic antagonists, they are free to overgrow and invade areas normally forbidden them. By periodic examination of the sputum and stools, antimicrobial-induced changes in the body flora may be detected in time to avert clinical superinfection.

Lincomycin. In vitro inhibition studies have indicated that the spectrum of activity of lincomycin (Lincocin®)[5–7] includes S. aureus and Staphylococcus albus, beta-hemolytic streptococcus, Streptococcus viridans, and Diplococcus pneumoniae but that the drug is not active against most strains of Streptococcus faecalis, Neisseria gonorrhoeae, or Neisseria meningitidis. Strains of S. aureus isolated from clinical material have been resistant to lincomycin, but the exact incidence of such resistance is not known at this time.

Untoward effects have included nausea, vomiting, abdominal cramps, and diarrhea. Loose stools are noted in about 15% of subjects receiving the drug, and diarrhea has required discontinuation of therapy in 2 to 3%. Rashes, stomatitis, epistaxis, headache, myalgia, pruritus ani, and vaginitis have been described. The drug also may be hepatotoxic, especially in patients who have underlying liver disease. Abnormal tests of liver function including elevated levels of serum transaminase have occurred in patients receiving the drug; whether jaundice has occurred as a consequence of administration of lincomycin is uncertain at this time. It is recommended that all patients receiving treatment for longer than one week have tests of liver function performed, and if results of the latter are abnormal, use of the drug should be discontinued. Since cases of leukopenia, including neutropenia, have been reported in patients receiving lincomycin, blood count should be monitored regularly. There appears to be no cross allergy with other drugs, including penicillin. Intramuscular preparations of the drug appear to be about as well tolerated as is procaine penicillin. Intravenous administration of lincomycin appears to be well tolerated. Therapy with lincomycin may result in overgrowth of nonsusceptible organisms, particularly yeasts. Safety for the use of lincomycin in pregnancy has not been established, and presently the drug should not be given to pregnant women or the newborn. It is also advised currently that the drug not be used in prophylaxis of rheumatic fever and in patients with preexisting renal, hepatic, endocrinal, or metabolic diseases until further data in such patients are accumulated.

CEPHALOTHIN

Cephalosporin C is an antibiotic elaborated by the fungus, Cephalosporium. By chemical removal and replacement of the aminoadipic acid side chain of cephalosporin C, semisynthetic compounds have been produced. The core of the cephalosporin molecule is 7-aminocephalosporanic acid. Of these partially synthesized cephalosporins, cephalothin (Keflin®) is commercially available.

A difficulty with cephalothin in the management of infections stems from an apparent dichotomy between in vitro bacterial susceptibilities and clinical results in certain cases in which the drug has been employed. That is to say, laboratory data would indicate that the drug is applicable in certain infections and yet clinical response is delayed, incomplete, or occasionally absent. Although such results may occur on use of other antibacterial agents, they appear to be sufficiently more frequent following employment of cephalothin as to warrant special attention until further clinical experience is obtained.

Untoward effects of cephalothin include thrombophlebitis when the drug is given intravenously for longer than two to three days, pain at the site of intramuscular injection, rashes, fever, serum sickness, anaphylactoid reaction, transient splenomegaly, transient neutropenia, eosinophilia, increased SGOT activity, and increased azotemia. Superinfection from Bacteroides, Klebsiella-Aerobacter, or Pseudomonas organisms occurs. Cross allergy between the cephalosporins and the penicillins is not entirely excluded; there is some evidence that a recent untoward reaction to a penicillin may predispose to an allergic reaction to cephalothin.

In patients having a propensity to fluid retention, such as cardiac or renal disease, it should be recalled that cephalothin is supplied as the sodium salt. The calculated sodium content of cephalothin is 55 mg. per gram.

Cephalosporin derivatives, while resistant to staphylococcal penicillinase, may be degraded by cephalosporinase. Cephalosporinase is an enzyme produced by certain gram-positive organisms (S. aureus, S. faecalis) and gram-negative bacilli (Salmonella, Aerobacter aerogenes). If the enzyme is productive of future clinical problems, such as contributing to bacterial resistance, there is the possibility of synthesizing cephalosporinase-resistant cephalosporins.

LESS COMMONLY USED ANTIBIOTICS

Bacitracin. This agent is primarily antagonistic to gram-positive organisms including most strains of S. aureus. It is not well absorbed on oral administration and must be injected intramuscularly for systemic effect. It has been used effectively in combination with other agents, such as chloramphenicol, against serious staphylococcic infections in which use of a single agent has not been so effective. With the availability of other effective antistaphylococcal agents, use of bacitracin systemically has declined.

In attempts to promote intestinal antisepsis, bacitracin administered by the oral route after operation has been recommended in patients who had received neomycin or other drugs before operation. Use of bacitracin in this manner is designed to eliminate the invasion by resistant staphylococci of the intestines that have been deprived of the normal bacterial flora. Oral bacitracin also has been used in cases of enteric amebiasis. Intracavitary instillation of the drug has occasional use.

Untoward effects after intramuscular administration of bacitracin include pain at the site of injection and nephrotoxicity which may be manifested by albuminuria, glycosuria, and azotemia. Nausea and vomiting are uncommon; urticaria is extremely rare. During intramuscular therapy, careful studies of renal function are imperative.

Vancomycin. This antibiotic must be administered intravenously against systemic infections. Formerly, its chief use was in patients with staphylococcal endocarditis who were allergic to penicillin, but currently cephalothin is preferred by some workers in such cases.

Vancomycin is not well absorbed when given orally and is applicable in the management of staphylococcal enterocolitis. The toxicity of the agent is largely, but not entirely, circumvented by virtue of its relative unabsorbability when given by the oral route.

Toxic effects that may follow administration of vancomycin, in addition to ototoxicity and phlebitis at the site of injection, include drug fever, chills, and anaphylactoid and dermal reactions. Renal function should be checked regularly in patients receiving the drug; in those with decreased function, vancomycin should be given in reduced amounts or not at all. Concurrent therapy with other ototoxic drugs should be avoided. Theoretically, prior therapy with potentially ototoxic drugs may increase the risk of ototoxicity on use of vancomycin.

Ristocetin (Spontin®). Like vancomycin, ristocetin probably is best reserved for staphylococcal infections that do not respond to more commonly employed antimicrobial agents, but currently the drug has infrequent clinical application. It may be of value in the treatment of enterococcal infections, especially in patients allergic to penicillin. Like vancomycin, the agent must be administered intravenously for systemic effect.

Side effects include phlebitis at the site of injection, drug fever, rashes, diarrhea, hematotoxicity (especially neutropenia and thrombocytopenia), and perhaps ototoxicity and nephrotoxicity. As with other antimicrobial agents, eosinophilia may indicate an impending untoward reaction to ristocetin. The incidence of untoward effects appears to parallel the size of the daily dose; less than 5% of patients have toxic effects if the daily dose is less than 1 gm., but almost 50% of patients have side effects when 5 gm. is given daily. The fact that a reduction of dosage may decrease toxicity, with return of depressed elements of the blood, has been considered more indicative of a direct hematotoxic effect on the bone marrow than of an allergic effect.

Cycloserine (Seromycin®). This drug has been used in conjunction with isoniazid and streptomycin in the treatment of selected cases of both pulmonary and extrapulmonary tuberculosis. It has also been recommended in the management of certain refractory infections, especially those of the urinary tract, due to E. coli and Klebsiella-Aerobacter and enterococcal and staphylococcal organisms. Pseudomonas and Proteus organisms often are resistant to the action of cycloserine. In certain patients having nocardiosis, cycloserine, when combined with a sulfonamide, may provide an enhanced therapeutic effect.

In patients with normal renal function. the maximal oral dosage should be 250 mg. of the agent every six to twelve hours, and preferably the latter. Persons of less than normal adult weight should receive comparatively smaller amounts of the agent. Blood concentrations of cycloserine in the range of 25 μg. per milliliter should not be exceeded, so that untoward effects may be minimized. Side effects are most likely to occur after administration of more than 1 gm. of cycloserine daily, particularly when the individual dose exceeds 250 mg. This dose (250 mg.) has been given two or three times daily for several months to patients having nocardiosis.

Untoward effects of cycloserine include dermatitis, headache, drowsiness, dizziness, mental confusion, hypomania, dyskinesia, and convulsions. The effects on the central nervous system generally appear within the first week or two of treatment. It has been reported[1] that untoward effects of cycloserine on the nervous system are prevented or controlled by concomitant administration of pyridoxine (vitamin B_6), either alone or in combination with anticonvulsants, tranquilizers, and sedatives. Cycloserine should be used with caution in patients who have impaired renal function and is contraindicated in patients with a history of epilepsy.

COMMENT

Antibiotics employed in the management of bacterial infections are a mixed blessing because their use may result in a diagnostic loss if they are utilized before diagnosis is established, they are expensive, and therapy with these drugs may result in various complications. These complications may be of such a nature as to disallow continued use of these drugs in a current situation and, as well, to negate their employment in future life-threatening infections.

Impaired renal function makes mandatory the careful use of certain drugs that may be complicated either directly by nephrotoxicity or indirectly by toxicity to other organ systems resulting from serum accumulation. When resistant organisms are encountered, the intrinsic severity of the infection is the keystone to deciding whether the risk associated with the use of more toxic drugs is justified. If renal function is less than normal, the doses of such drugs should be correspondingly reduced.

Bacterial resistance is a complication per se since it may result in a drug being inapplicable to a given infection. In addition, bacterial resistance is a necessary factor in the genesis of the complication of superinfection. Bacterial resistance may reflect not only therapy with a specific drug but of kindred drugs because of the ramifications of bacterial cross resistance. Since bacterial resistance appears to be a direct function of the total amount of a drug, or allied drugs, used in a given environment, therapeutic discrimination is mandatory. In regard to superinfection, periodic microbiologic study of the sputum and stools during therapy may reveal floral changes in time to avert clinical manifestations of superinfection.

The seriousness of some of the potential complications of antibiotic therapy employed in bacterial infections makes it incumbent on the practicing physician to be familiar with the causative drugs and to utilize them in a selective manner.

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MENSES and breast development in children with constitutional precocious puberty can be controlled by long-acting intramuscular medroxyprogesterone acetate (Depo-Provera®). The short-acting oral preparation is less effective. In 5 patients less than 4 years old with constitutional precocious puberty, oral Depo-Provera® controlled bleeding in 3 and decreased breast size in 2. The long-acting parenteral preparation controlled bleeding in 4 and diminished breast size in 3; pubic hair appeared in 3, diminished in 1, and remained unaltered in 1. Accelerated skeletal maturation and rapid increase in height were not affected during ten to twenty-four months of treatment.

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Current Concepts of Radiation Biology as Relevant to Radiation Therapy

YOSH MARUYAMA, M.D.
Minneapolis

RADIATION THERAPY and surgery represent the only modalities of treatment which offer significant likelihood of curing malignant disease. The basic approach of surgery is simply to excise all areas involved by tumor, along with contiguous areas in which tumor extension is likely. This basic approach is modified in radiotherapeutics by the consideration that all tumor-bearing tissues should be irradiated to the limits of their tolerance, including the adjacent areas of probable involvement, while inflicting a minimum of damage to the surrounding normal tissues. The en bloc approach is fundamental to both. The use of radiotherapy is limited when: [1] the disease is beyond the field of irradiation, that is, distant metastases are present, [2] the quantity of tumor present exceeds that which can be controlled by doses of irradiation within the tolerance of the surrounding normal tissue, and [3] there is inadequate radioresponsiveness of certain tumors. It is of interest to ascertain the factors governing radioresponse, with the hope that experimental radiobiology may elucidate mechanisms to improve radiotherapeutic effectiveness.

TRADITIONAL CONCEPTS OF RADIOSENSITIVITY

There is a wide belief that different cells and tissues vary widely in their intrinsic susceptibility to ionizing radiation. Introductory chapters of all textbooks of radiation therapy indicate hierarchies of tissues of varying radiosensitivity, and some estimates place these differential sensitivities in ranges of 1,000-fold between different tissues. These conclusions are drawn largely from whole animal radiation biology. As early as 1906, Bergonie and Tribondeau of the French radiobiological school postulated a law of radiosensitivity. It states that "X-rays are more effective on cells which have a greater reproductive activity; the effectiveness is greater on those cells which have a longer dividing future, and on those cells whose morphology and function are least fixed." This well-known law, with only a few exceptions, still holds to this day. One of the fundamental statements of this law is that cells that divide are those that undergo the most marked effects of ionizing X-rays. Mitotic suppression and division delay occur following irradiation, and both contribute to the inhibition of cell growth and proliferation (Fig. 1A and B).

MODE OF CELL DEATH

It has been repeatedly confirmed that one of the primary effects of X-radiation is on cell division and various mitotic processes and that cell death usually takes place during mitotic division. We now know that cell death can take place following X-radiation by at least 3 different mechanisms: [1] intermitotic, affecting cells such as the neuroblast, the small lymphocyte, and the spermatogonium or oocyte, [2] mitotic, the mechanism which takes place with most cell types following radiation, and [3] combined mitotic and intermitotic, affecting cells such as the malignant lymphocyte or germ cell. The first is associated with prompt pyknosis of the cell nucleus, leading to karyohexis and cell dissolution shortly after injury. The second is a manifestation of the inability of the injured cell to continue to successfully undergo mitotic division and is eventually expressed by a complete failure to divide. The third, an uncommon form, is a combination of both the above mechanisms. Cell death can be a slow process and may require weeks, during which time the cell looks morphologically intact but is incapable of further division. On the other hand, leukemic deposits, neuroblastomas, and lymphomas, for example, may respond so promptly that they literally are "melted away" by radiation. This feature is due, in part, to the mode of prompt intermitotic cell death. A second feature of tumor lysis following irradiation is dependent on the rate of cell divi-

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YOSH MARUYAMA *is assistant professor of radiology, University of Minnesota Hospitals, Minneapolis.*

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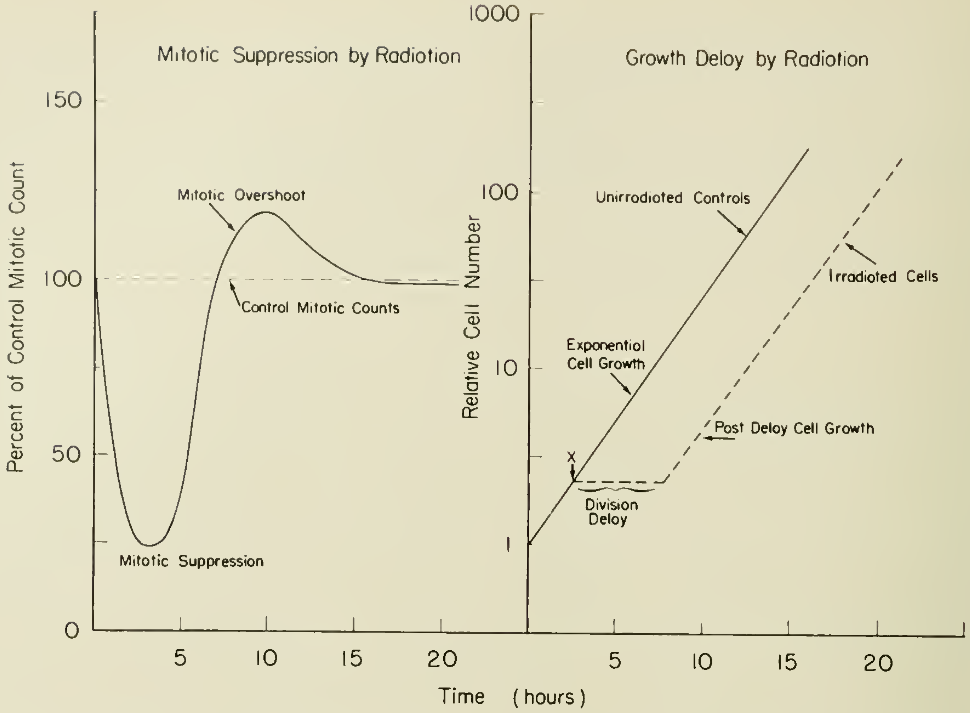

Fig. 1. Shows (A) mitotic suppression and (B) growth delay which occurs after irradiation. X = irradiation event

sion. Thus, even though a lethally damaged cell can undergo one or more successful divisions, it will eventually undergo lysis. The rapidity with which this process will occur is dependent on the rate at which the tumor cells are dividing, or the cell generation time. Cells that do not divide may never show lethal injury, such as brain or liver, while rapidly dividing cells may show early dissolution in accordance with the previously cited law. However, nondividing tissue may express latent radiation injury when provoked into growth, such as by partial hepatectomy in the case of liver tissue.

MODERN CELLULAR RADIOBIOLOGY

Gross tumor responses are largely a function of mode of cell death and cell proliferation kinetics. The responses of single isolated mammalian cells accurately and quantitatively assessed came from the investigations of Puck and Marcus[1] in 1956. These workers developed methods for culturing single cells in vitro, essentially as single organisms, attached to the surface of a Petri dish. Single cells then could give rise to macroscopic clones of descendents by continued cell division. If such cells were exposed to ionizing radiation, certain proportions of the cells would fail to form macroscopic clones. This led to the concept that the proliferative capacity or reproductive integrity of the cells has been altered. This concept now is widely accepted as basic in defining the action of radiation on cells and radiosensitivity. In short, only those cells which survive the injury and which retain the capacity for

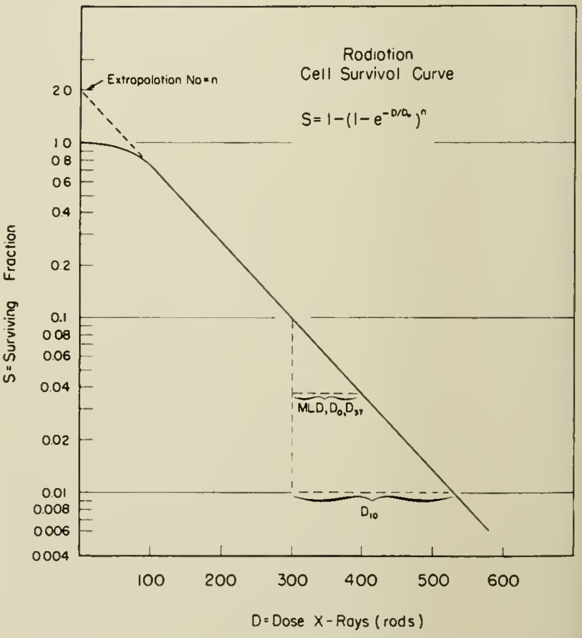

Fig. 2. Survival curve, representing a semilog plot of surviving fraction against X-ray dose. S = surviving fraction, MLD = median lethal dose, n = extrapolation number

unlimited division will cause, for example, regrowth of a tumor. To be distinguished is functional activity, which may be quite unaltered even after a cell is lethally injured.

FORM OF THE DOSE RESPONSE CURVE

Figure 2 shows the response curve similar to that obtained by Puck and Marcus for X-rays. This is known as a survival curve and represents a semilog plot of surviving fraction against X-ray dose. On a linear plot, the same curve would be a continuously curving one, nearly approaching, but never quite reaching, the abscissa. Several of its features are notable: [1] an initial shoulder region, [2] a linear exponential portion characterized by a slope, which is called the median lethal dose, D_0 or D_{37}, and is the dose to reduce the survivors along this portion by 37%, and [3] an extrapolation number, or the intercept of the straight line portion with the ordinate axis at zero dose.

This dose-response survival curve is similar for virtually all cell types studied in vitro with a variety of cells from both normal and malignant tissues of man as well as for a wide variety of species, such as a hamster ovary or mouse fibroblasts. There is an initial shoulder region of 50 to 75 rads (radiation absorbed dose) in which the dose can be accumulated without loss of viability, and the extrapolation number is greater than 1. This form of survival curve is described as "multihit," implying that several sensitive targets must be "hit" for the cell to be inactivated.

Finally, it has been shown that cell death may occur during cell division. But many cells, rather than dying, continue to grow into so-called giant cells, 7 to 10 times larger than normal cells and often multinucleated. Moreover, the lethally injured cells may complete one or more postirradiation divisions before undergoing dissolution.

The concept of differential intrinsic radiosensitivity of various tissues was finally dispelled as a consequence of this and related work, as the slope of the killing curve, defined by the D_{37} dose, was similar for all cells and tissues studied and lay between 100 and 200 rads.

IN VIVO MAMMALIAN CELL RADIOBIOLOGY

These studies were performed in vitro. Hence, there was the possibility of distortion through the artificiality of the growth conditions, and the relevance for the in vivo situation was questioned. Recently, methods for in vivo quantitative cell biology have been developed. They measure radiosensitivity in terms of the loss of reproductive integrity of the irradiated cells.

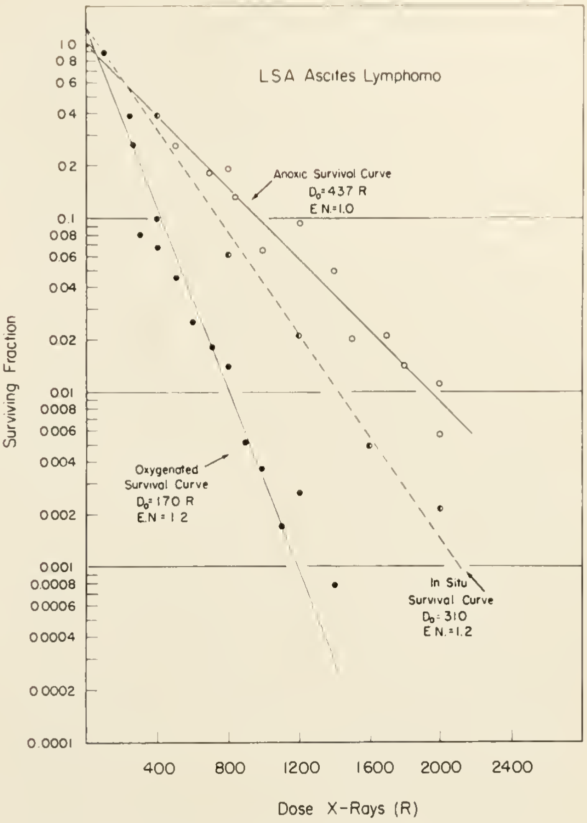

Fig. 3. Response of mouse ascites lymphoma cells to X-irradiation. EN = exponential number

MURINE LEUKEMIC CELLS

Hewitt and Wilson[2] studied a spontaneous leukemia of an inbred line of mice. Hewitt found that by inoculating known numbers of malignant leukemic tumor cells, he would be able to arrive at a point where a measured number of such cells would produce tumor "takes" in half the inoculated recipient mice. A "take" here is defined as death of the recipient mouse by disseminated tumor, such as is seen with leukemia. That cell number producing tumor "takes" in half the recipients is called the 50% tumor dose or TD50. In their experiments, living animals with tumor were exposed to graded doses of whole body cobalt (Co^{60}) gamma rays. The cells were harvested (obtained by mincing up the liver and taking the tumor cells present in the supernatant fluid), made into single cell suspensions, and then reinoculated into isogenic mice. These mice then were observed for a sufficient period of time until it was certain that all mice who received reproductively viable cells would have developed tumor. After X-irradiation, it is obvious that a larger number of cells must be inoculated in order to get half the animals to die of tumor. Thus, by comparing the TD50 values, one can determine the surviving fraction for each X-ray dose.

Such a survival curve is shown in Figure 3. The data were obtained using an ascites lymphoma of C57BL mice according to the method of Hewitt, and a survival curve was obtained similar to cells irradiated in vitro. There is a small shoulder, an exponential portion, where the D_0 is 160 rads of 250 KVP (kilovolts peak) X-rays and an extrapolation number of 1.2. These values are similar to those obtained by Hewitt and Wilson. By irradiating the cells in vitro, we can obtain exactly the same values. Therefore, the response of the cells either in vitro or in vivo is identical.

The upper curve shown was obtained when the cells were irradiated in dead mice and, again, is similar to the observations of Hewitt and Wilson. Using their ingenious method, the cells were rendered fully anoxic, and it is apparent that the killing curve is now much less steep. In fact, for a reduction of the cell number from 100 to 10, it now requires a much larger dose of X-radiation. In comparing the D_{37} values, we found that the anoxic curve has a slope which is 2.6 times less steep ($D_{37} = 410$ rads) and therefore much more radioresistant. This effect is the well-known "oxygen" effect, and the oxygen enhancement ratio has been observed to lie between 2 and 3 in a wide variety of systems.

Figure 3 shows the response of ascites lymphoma cells irradiated in vivo after a much larger volume of ascites had formed. Compared with the oxygenated and anoxic curves shown, it is evident that the killing slope is now intermediate. This indicates that cell hypoxia in the living animal can be a real problem, depending, for example, on distance from blood vessels, necrosis, edema, volume of ascites, and so forth.

NORMAL CELL RADIOSENSITIVITY (BONE MARROW "STEM" CELLS)

What about normal cell radiosensitivity in vivo? Till and McCulloch[3] found that, if bone marrow cells were injected intravenously, a certain proportion of the cells would arrive in the spleens of the mice and there proliferate to form macroscopic colonies or nodules which are readily countable by eye. If one compares the number of nodules before and after irradiation of the cells, either in vivo or in vitro, then one can determine the number of reproductively intact, surviving colony-forming cells (CFU) which remain after exposure to ionizing radiation.

An example of such a survival curve is shown in Figure 4. The data again show that the survival curve for the CFU of normal bone marrow, and these are presumably the stem cells, is exactly like that of all other mammalian cells studied. Here the D_{37} is 104 rads for 250 KVP X-rays, with a small shoulder and an extrapolation number of 1.1. The lower curve shows the effect of high linear energy transfer (LET) radiation which, in this case, was fast neutrons of average energy—6 million electron volts. It is evident that, for the fast neutrons, the D_0 is greatly reduced and in these experiments was 40 rads or 2.5 times less than that of 250 KVP X-rays. This ratio is called the relative biological effectiveness or RBE. High LET radiation, such as fast neutrons, is much more effective in destroying cells, dose for dose, because of heavy ionization along the track of the particle. Moreover, the survival curve shows no shoulder, or more simply, it is single-hit. This means that the cells do not accumulate injury before killing occurs but, instead, die with a single interaction of radiation and target.

SURVIVAL TIME SURVIVAL CURVE

Recent work[4] has shown that, following the inoculation of a known number of leukemic tumor cells into isogenic mice, the recipients will live for known intervals of time. By irradiating

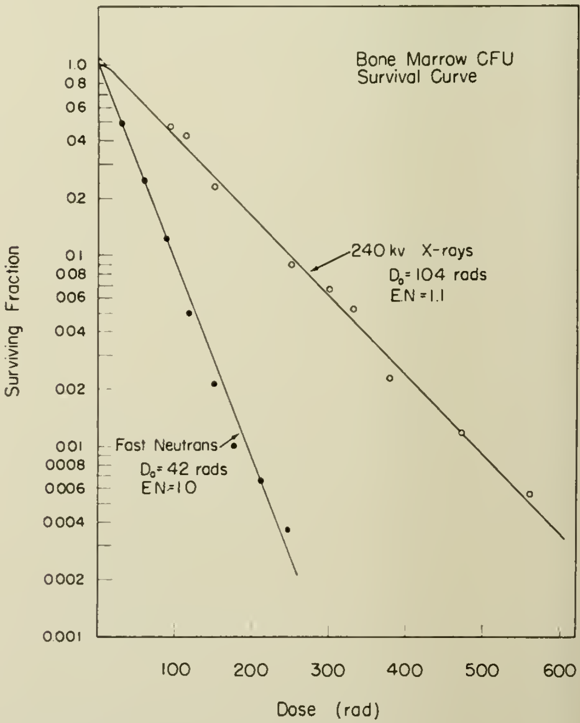

Fig. 4. Survival curve of colony-forming cells (CFU) of normal bone marrow. EN = exponential number

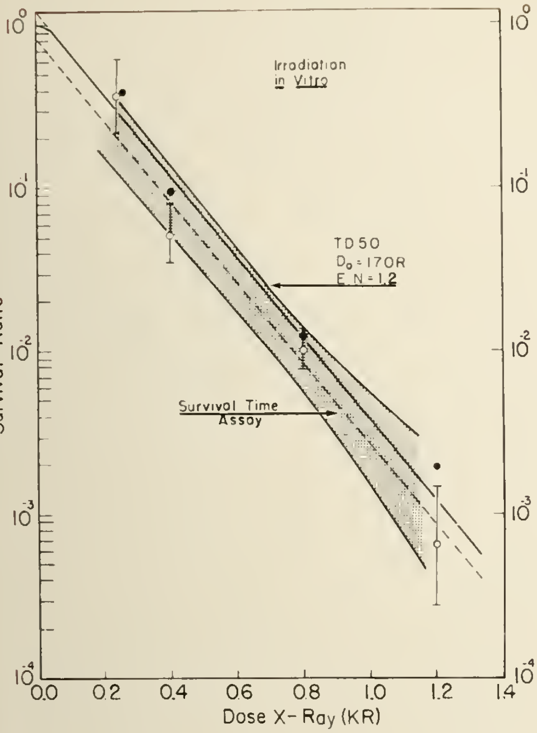

Fig. 5. Comparison of TD50 survival curve (solid line and closed circles) and survival time response curve (dashed line and open circles) for in vitro irradiation of mouse leukemic cells

the leukemic tumor cells in vitro (oxygenated), in vivo (hypoxic), or in dead mice (anoxic), we found that, despite being inoculated with large numbers of tumor cells, the animals live for varying intervals, depending not on the apparent number inoculated but on those cells that survive the radiation event, that is, the surviving fraction. The same cells can be used to determine the surviving fraction by the method of Hewitt, and the results (Fig. 5) conform with expectation.

These data represent convincing evidence that the response of single cells to ionizing radiation is characterized by a near exponential survival curve. Thus, intrinsic radiosensitivity is similar for all mammalian cells, but the expression of this injury, or radioresponse, is dependent on [1] mode of cell death, [2] the mitotic rate of the cells, [3] the tumor cell oxygenation, and possibly other factors which are still poorly understood. Survival curves for mammalian cells have been shown to be exponential for at least six decades of killing.

SIGNIFICANCE OF SURVIVAL CURVES TO RADIOTHERAPY

Another convenient value is the D_{10}. This is the dose to reduce the original cell number to 10% of its original number, as determined by the exponential portion of the survival curve and is 2.3 $\times D_{37}$. After delivering such a dose, we can expect to kill 90% of the cells; 2 such doses as a single exposure would kill 99% of the cells. Similarly, 6 D_{10} doses destroy 99.9999% of the cells or, in other words, 1 cell in a million will survive the irradiation event.

Let us now consider a hypothetical tumor. If the tumor is exactly 2 cc. in size and the tumor cells are 10 μ in diameter, then the number of cells in this tumor will be approximately 2×10^9 cells. If the tumor is half stroma, then there are exactly 1×10^9 tumor cells present. From survival curve data, let us try to destroy every single tumor cell. From survival curves, for a D_0 of 110 rads, the D_{10} is about 250 rads. To kill 10^9 cells requires $9 \times D_{10}$ or 2,250 rads. The statistical probability of destroying 10^9 cells follows a Poisson distribution at the 1-cell level. Let us give enough to destroy 10^{10} cells or 2,500 rads. At this dose, there should be 90% cures (see the table). The important point is that each single tumor cell must be destroyed to cure the tumor. If we do not, then the survivors will regrow the entire tumor in course of time. It also follows from such survival curve considerations that larger tumors may require appropriately larger doses of radiation.

SUPPORTING CLINICAL DATA

The report of Hale and Holmes[5] from the Massachusetts General Hospital, where treatment for squamous and basal cell carcinomas of the skin mainly consists of single exposures of low voltage X-rays, is considered relevant to answering this question. Of 370 lesions treated by single doses in the range of 2,400 to 2,800 rads, there were 32, or 9%, failures. They further note that, in 949 tumors 2 cm. or less in diameter, there were 110 failures, or a 12% incidence of failure to cure. Considering this range of doses and only estimating the magnitude of the tumor cell num-

DOSE-RESPONSE RELATIONSHIP FOR A HYPOTHETICAL TUMOR EXHIBITING A D_{37} OF 110 RADS

Initial cell number	*Single exposure dose (rads)*	*Number retaining reproductive integrity*	*Probability of local cure*
10^9	250	10^8	0.0
10^9	500	10^7	0.0
10^9	750	10^6	0.0
10^9	1,500	10^3	0.0
10^9	2,250	10^0*	37%
10^9	2,500	10^{-1}†	90%‡

*One cell
†Ten cells in 100 such tumors would remain viable
‡Ten percent local failure rate

bers to be about 10^9, with the limitations mentioned earlier, there is rough agreement between survival curve parameters and actual clinical observation. Therefore, real and tangible meanings, relevant to tumor radiotherapy, can be derived from survival curve theory.

CELLULAR RECOVERY AND REPAIR

It is well known from early clinical experience and from radiobiological experiments that fractionated doses of radiation are better tolerated than single massive exposures. Essentially, the net effect of a given dose delivered in two fractions was never so great as when it was delivered singly. Elkind and Sutton[6] have further defined this recovery process in terms of the behavior of single cells. Thus, single mammalian cells exhibit multihit survival curves; that is, they exhibit a threshold region over which sublethal damage can be accumulated before any effect is evident. Between fractionated doses delivered approximately eighteen hours apart, they observed that full recovery occurs and that repeated cycles of recovery take place following repeated injury by radiation spaced approximately twenty hours apart. Elkind further described a characteristic and well-defined structure to this recovery process. First, there is a prompt and rapid early "repair" of this injury which reaches a maximum in two to three hours. This early repair process can be reduced by low temperatures or by actinomycin D but takes place under hypoxic conditions. Second, there is a decline after the first maximum which falls to a minimum at about six hours and then rises again to full recovery by about eighteen hours. During this cycle of injury and recovery, there is a disappearance and reappearance of the threshold region of the survival curve, manifested by a fall and rise in the extrapolation number, with the second rise probably on the basis of cell division. One of the major features at the cellular level of the observed decline in the net effect by fractionation is on the basis of this "recovery" process.

Another feature of recovery and repair must be added for the intact animal. This feature can be described as repopulation of the irradiated field from elements of tissue adjacent to the field of injury. Epithelium regenerates and migrates centripetally from the nonirradiated margins, and stromal and totipotent mesenchymal cells migrate into the irradiated region from adjacent and remote parts of the host. The radiotherapeutic principle of radically irradiating the tumor-bearing tissues while subjecting a minimum volume of adjacent normal tissues to radical dosage, thus, is logical to permit full restoration of the normal tissues.

CELL CYCLE AND RADIOSENSITIVITY

Since the advent of microautoradiography, it has been possible to study the cell cycle in both the mitotic and intermitotic phases. The mitotic phase is short, relative to the interphase period. For example, whereas mitosis may take one hour, interphase may be ten to twenty hours or even longer, such as in nerve cells. Tritium-labeled compounds, especially H 3-thymidine, have dissected the interphase period into 3 distinct periods: [1] The G_1 or postmitotic, predeoxyribonucleic acid (DNA) synthetic, [2] the S or DNA synthetic, and [3] G_2 or post-DNA synthetic, premitotic phase (Fig. 6). During the S phase, the cell nucleus would become labeled and a cell would build a double complement of DNA which, during mitosis, would be equally divided between 2 identical daughter cells. It is now known, from experimental work done with cells whose cycles have been synchronized, that the radiosensitivity of single cells fluctuates during the different phases of the cell cycle.[7] The direction and pattern are variable according to the cell type under study and can involve either the extrapolation number, the D_{37}, or both. Therefore, the overall population response of an asynchronous population would be the average of all the cells present and the distribution of the cells in the various compartments of the intermitotic and mitotic cycles.

THE NATURE OF THE INTRACELLULAR TARGET

The nature of this "target," which resides in the cell and determines the response of the reproductive integrity to ionizing radiation, has received extensive study in recent years. Earlier microbeam irradiation of cells done by Zirkle and his associates[8] showed that the nucleus was much more sensitive than any other intracellular structure. Recent work by Djordjevic and Szybolski[9] and Kaplan and his colleagues[10] has shown that the sensitive target material can be localized even more precisely to certain macromolecules that reside in the nucleus. These are the nucleic acids and, more specifically, the deoxyribonucleic acids. These macromolecules are a double helical structure composed of a sugar, phosphate, and 4 bases, of which 2 are purines and 2 are pyrimidines. One of the pyrimidine bases is thymidine and, in certain analogues of thymidine, halogen is substituted in place of the methyl group (Fig. 7). These analogues look just like thymidine and, because of this similarity, can enter DNA in place of thymidine, the normal constituent.

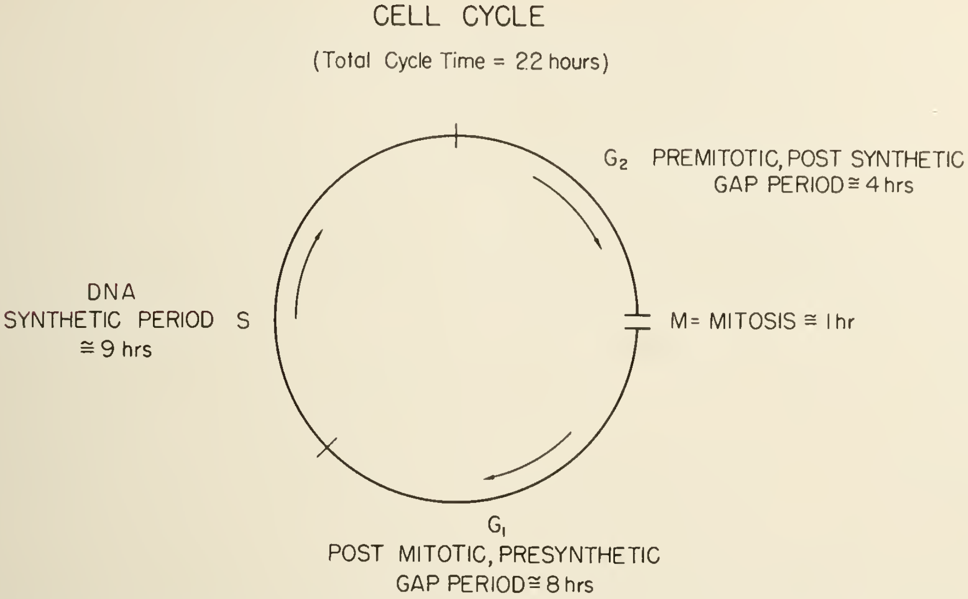
CELL CYCLE
(Total Cycle Time = 22 hours)
G_2 PREMITOTIC, POST SYNTHETIC GAP PERIOD ≅ 4 hrs
M= MITOSIS ≅ 1 hr
G_1 POST MITOTIC, PRESYNTHETIC GAP PERIOD ≅ 8 hrs
DNA SYNTHETIC PERIOD S ≅ 9 hrs

Fig. 6. The interphase period of a cell cycle, including mitotic and intermitotic phases, in this example totaling twenty-two hours

They do not enter into any other class of molecules within the cell. Once incorporated, certain properties of the cell are altered and one of the most striking is the response to ionizing radiation. It has been established that this same radiosensitization occurs for bacteria, mammalian cells in culture, mammalian cells in vivo, bacteriophages, and for a wide variety of cells from diverse species and tissue origins. Some of the evidence for DNA as the target material can be summarized as follows:[11]

1. DNA viruses which are composed of only 2 components—protein and DNA—can be sensitized by the thymidine analogues.

2. The degree of sensitization can be correlated with the degree of replacement of the thymidine of DNA.

3. As a transforming principle, it can enter another bacterial cell of appropriate competence, carrying with it genetic information; it can be labeled with the analogues, irradiated either in vivo or in vitro, and used in transformation studies. Radiosensitivity is transferred with such transforming principle.

4. Other evidence, such as with purine analogues, correlation of base composition with radiosensitivity, nucleotide content, ploidy, and so forth, implicates DNA as the primary target of reproductive integrity.

CONCLUSION

Recent evidence has been reviewed on the response of mammalian cells to ionizing irradiation. This evidence indicates that the response of single mammalian cells in vitro and in vivo is characterized by a near exponential survival curve, similar to all other single cell systems studied. The radiosensitivity of single cells, as defined by the response of reproductive integrity or proliferative capacity to ionizing radiation, is similar for mammalian cells of diverse tissues and species origin. Radioresponse is a function of the intrinsic radiosensitivity, local tissue and cell oxygenation, the mode of cell death, and the mitotic rate of the cells.

Local radiation control of a tumor in vivo is the sum total of at least 2 major and 3 minor components. The 2 major components are: [1] cell killing, that is, the loss of reproductive integrity or proliferative capacity, and [2] growth inhibition. The latter is due to mitotic suppression, division delay and, in some cases, to alteration in the cell growth kinetics. Provided few

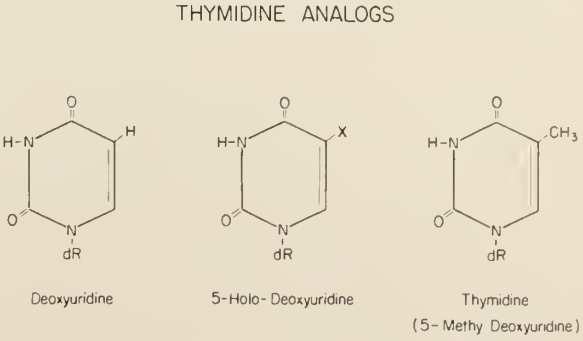

Fig. 7. Structural formulas of thymidine analogues

viable survivors remain and proliferate slowly, a local recurrence may never be seen during the lifetime of the host. Division inhibition may be associated with the formation of giant cells. The 3 minor components are: [1] immunological, due in part to the release of lethally damaged cells to incite the immunological responses in the host, implying antigenic dissimilarities between normal and tumor cells, [2] vascular, due to alterations to the vascular supply, and [3] abscopal effects, acting through complex factors and possibly humoral agents from remote sites in the host animal. The 3 latter factors are still poorly understood and may be of little or no significance.

"Radioresponse," as viewed by the clinician, is the gross response of tumors and is the commonly used criterion in the use of the term "radiosensitive." It is obvious that neither is in any way related to "radiocurable," which is dependent on the inherent biological behavior of a particular tumor. It is anticipated that, as further understanding of basic radiobiological mechanisms emerges, a decreased primary failure rate will be observed and extension of radiotherapy to tumors hitherto considered radioresistant will be possible.

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IMMEDIATE REMEDIAL ACTION is required in suspected rupture of an aortic graft into the small intestine. Primary reresection and prosthetic reconstruction of the aorta is preferable. Delay is risky with peptic ulcer symptoms and in backache, especially with previous aortic surgery. Massive gastrointestinal bleeding and shock are indicated and a pulsatile abdominal mass confirms diagnosis of false aneurysm with aorticointestinal fistula.

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Guanethidine — A Potentiator of the Bronchodilator Effect of Epinephrine in Chronic Bronchial Asthma

GAMAL E. MEGAHED, M.D., and M. S. FAHMY, M.D.
Cairo

INTRODUCTION AND AIM OF WORK

When the sympathetic nerves to smooth muscles are severed, the denervated muscles develop greatly increased sensitivity to the transmitter substances normally released at the nerve endings. The degree of hypersensitivity of the smooth muscle is materially less if the preganglionic rather than postganglionic nerves are sectioned, according to Rushmer.[1]

Ganglion blockers were shown by Hirshleifer and associates[2] to potentiate the effect of epinephrine in 10 patients with epinephrine-fast bronchial asthma.

Guanethidine (Ismelin®) is a specific peripheral sympathetic nervous inhibitor. The compound shares, in common with the ganglion blockers, the property of enhancing the pressor effect of exogenous catecholamines.[3-6] Abboud and associates[7] suggested Ismelin® may have a direct action on the receptors which increase their sensitivity to norepinephrine.

METHODS AND MATERIALS

Twenty patients with chronic, extrinsic, noninfective bronchial asthma which did not respond favorably to administration of epinephrine, were selected for the present study. There were 16 males and 4 females, of an average age of 29 years. The minimum duration of asthma was four years and the maximum was nineteen years. All had the following features in common:

> During the early period of the disease relief was obtained by simple oral bronchodilator tablets of ephedrine, aminophylline, and phenobarbital which minimized severity of the attacks and prolonged the intervals beween attacks. Acute paroxysms were relieved by subcutaneous epinephrine or intravenous aminophylline.
>
> Later in the course of the illness, the respiratory difficulty became almost continuous with severe, acute exacerbations. At first several doses of subcutaneous epinephrine and intravenous aminophylline daily gave short lasting relief, but later failed to do so. This clinical lack of response to epinephrine administration constituted a basic feature in the selection of our patients.

Eight of these patients had a history of steroid therapy, which they stopped without medical advice on obtaining reasonable relief of their respiratory difficulty. Severe relapses resulted. The asthma in all 20 patients was of severity sufficient to indicate steroid therapy. Steroids were not prescribed, however, because continuation of therapy under medical supervision for a reasonable interval after hospital discharge could not be arranged.

Each patient was given a set of pulmonary function tests after a light breakfast. Every test was repeated several times and the best result was chosen.

The apparatus used was an improved simple spirometer (Godart's Expirograph). It has a counterbalanced light bell of 9 liters capacity. Its cross-sectional area is 300 cm.^{2} and, therefore, a movement of 1 cm. is caused by 300 ml. of air. The movements of the bell are recorded on a kymograph having 3 speeds: 30 mm. per minute for the vital capacity, 60 mm. per minute for the maximum breathing capacity, and 1,200 mm. per minute for the timed vital capacity.

This apparatus has several advantages. (1) The inertia of the moving parts is minimized by the small mass of the bell and the reduced velocity and acceleration of the bell because of

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GAMAL E. MEGAHED *and* M. S. FAHMY *are with the Medical and Pulmonary Function Units, Faculty of Medicine, Cairo University.*

its large cross-sectional area. The bell does not have to move far to accommodate the respired air and, therefore, the velocity is similarly reduced for any rate of air flow. (2) The tendency of the water column to resonate is minimized by the diminished excursions of the bell which reduce the length of the water column through which it moves, and by the damping of the oscillatory movement of the water due to reduction of the total mass of water inside the bell to the minimum in relation to the mass of water outside. (3) The resistance to airflow is minimized by the wide tubing and the low resistance valves.

The following set of pulmonary function tests were performed for each of the patients:

The vital capacity (V.C.) The patient in the standing position was asked to inspire as deeply as possible and then to expire fully. The volume was corrected to body temperature, pressure, and saturation. The result was expressed in milliliters and as percent of predicted V.C. The predicted values were calculated from height, weight, and sex. The surface area was obtained from the Dubois body surface charts prepared by Boothby and Sandlford of the Mayo Clinic.

The timed vital capacity (T.V.C.) The same procedure as in V.C., but with the kymograph running at 1,200 mm. per minute. The patient was asked to expire as rapidly and fully as possible until the tracing reached a base line. The expirograph obtained was calibrated for the time; each of 2 cm. of the horizontal lines being equivalent to one second. The expired volume in each of the first three seconds (FEV_1, FEV_2, FEV_3) was calculated and expressed as a percentage of the actual V.C. of the patient.

The forced expiratory time (F.E.T.).

The maximum breathing capacity (M.B.C.) The patient, while standing, was asked to breathe for fifteen seconds as deeply as possible and at a rate ranging from 48 to 60 breaths per minute. The M.B.C. was calculated by converting the volume of breathing in fifteen seconds into volume per minute and then correcting to body temperature, pressure, and saturation. The results were expressed in liters per minute, as well as a percent of the predicted M.B.C. The predicted values were obtained from body surface, age, and sex charts done by Baldwin and associates[8] in 1948.

The air velocity index (A.V.I.) This was calculated as described by Gaensler[9] in 1950 as the percent of the predicted M.B.C. divided by the percent of the predicted V.C.

Each patient was then given a subcutaneous injection of 0.3 mg. epinephrine. To evaluate the bronchodilator effect, these pulmonary function tests were repeated thirty minutes after the injection and the degree of change in each of the tests applied was then estimated. Neither the subjective impressions of the patients nor their physical examinations were relied upon in the evaluation since both are known to be unreliable and bear little quantitative relationship to the severity of bronchospasm.[10]

The patients were given oral aminophylline cachets, 3 times daily, and after four days the same set of pulmonary function tests was repeated before and after epinephrine. Comparison of the degree of change, before and after oral aminophylline, showed no significant variation. The higher change, however, scored by each patient in each individual test, was taken as the control value. Oral aminophylline was continued all through the period of the study. No other medications were given.

Each patient was then given 12.5 mg. Ismelin® each morning for seven days. On the last

TABLE 1

CHANGE IN DIFFERENT PULMONARY FUNCTION TESTS AFTER EPINEPHRINE

Test		*Mean change*	*Standard deviation*
Increase in M.B.C. (liters per minute)	A	9.9	12.7
	B	14.9	12.2
	C	16.1	15
Increase in M.B.C. (percent of control)	A	24.6	42
	B	24.6	21.2
	C	29.5	46.5
Increase in FEV_1 (percent of V.C.)	A	7.25	6.3
	B	7.4	7.2
	C	6.15	8.1
Increase in FEV_2 (percent of V.C.)	A	4.45	6.3
	B	6.5	5.9
	C	5.12	6.75
Increase in FEV_3 (percent of V.C.)	A	3	3.3
	B	6.02	6.75
	C	3.78	5.76
Decrease in F.E.T. (seconds)	A	0.9	1.37
	B	1.51	1.69
	C	0.59	0.77
Increase in V.C. (liters)	A	0.15	0.13
	B	0.08	0.14
	C	0.14	0.14
Increase in A.V.I.	A	0.1	0.17
	B	0.152	0.13
	C	0.14	0.14

A. Without treatment—20 cases

B. Under treatment with Ismelin®—20 cases

C. Under treatment with Ecolid®—14 cases

TABLE 2

Test		*Cases showing significant change after epinephrine* *No.*	*Percent*	*Cases showing no significant change after epinephrine* *No.*	*Percent*	*Total 100%*	*Chi square*	*Probability*
M.B.C.	A	7	35	13	65	20	4.9	Less than 0.05
	B	15	75	5	25	20		
A.V.I.	A	7	35	13	65	20	5	Less than 0.05
	B	15	75	5	25	20		
Battery of all tests	A	12	60	8	40	20	5	Less than 0.05
	B	19	95	1	5	20		

A. Before treatment

B. Under treatment with Ismelin®

day the same set of pulmonary function tests was performed before and thirty minutes after the subcutaneous injection of epinephrine, and the degree of change in each of the tests applied was determined.

After a week, with no other treatment except the aminophylline cachets to eliminate the residual effects of Ismelin®, each patient was then given 12.5 mg. chlorisondamine chloride (Ecolid®), a ganglion blocker, 3 times daily, for seven days. Six patients did not complete this period, 2 because of pneumonitis and 4 because of severe postural hypotension which necessitated stopping the drug. These patients were excluded from this part of the study. On the last day the same set of pulmonary function tests was performed on the remaining 14 patients, before and thirty minutes after the subcutaneous injection of epinephrine.

The degree of change after epinephrine was compared under the 3 different conditions of the study, namely: without treatment, treatment with Ismelin®, and treatment with Ecolid®.

The least significant change in each of the pulmonary function tests after epinephrine was statistically computed. The number of cases which showed significant change after epinephrine were compared under the 3 different conditions of the study using the chi square (χ^2) test.

The mean change in each of the pulmonary function tests after subcutaneous epinephrine under the 3 different conditions of the study is shown in Table 1.

Statistical comparison of the mean changes showed that with the exception of the FEV_3 the difference under the 3 conditions of the study was not statistically significant. The difference between the mean increase in the FEV_3 after epinephrine, under Ismelin®, (6% of the V.C., with a standard deviation of 6.8%), was found by statistical analysis using Student's T-test, to be significantly higher than the mean increase in FEV_3 after epinephrine, before treatment (3% of the V.C. with a standard deviation of 3.3%), P 0.02. The difference between the mean increase in the FEV_3 after epinephrine, before treatment, and under treatment with Ecolid®, however, was not statistically significant.

Statistical analysis of our studies indicates that after administration of epinephrine significance can be ascribed to:

1. Rises in the M.B.C. equivalent to 19 liters per minute, or 26% of control
2. Increase of 600 ml. in the V.C. or 16.6% of predicted V.C.
3. Increase in the FEV_1 equal to 8.5% of the V.C.
4. Increase in the FEV_2 equal to 7.1% of the V.C.
5. Increase in the FEV_3 equal to 13.8% of the V.C.
6. Decrease in the F.E.T. equal to 1.5 sec.
7. Increase in the A.V.I. of 0.1

We applied these criteria of the least significant change under the effect of epinephrine to our data for all the tests, with the exception of the M.B.C., for which we used the criterion suggested by Snider and associates[10] in 1952. They ascribed significance to rises of 20% in the M.B.C. when the control is less than 50 liters per minute and considered rises of 10 liters per minute significant when the control M.B.C. is greater than 50 liters per minute.

Application of these criteria to our data enabled us to detect the number of patients who showed significant change after the administration of epinephrine in each of the pulmonary function tests applied under the 3 conditions of the study, namely, without treatment, under treatment with Ismelin®, and under treatment with Ecolid®. The combination of pulmonary function tests permitted detection of a greater number of cases showing significant change than any single test did.

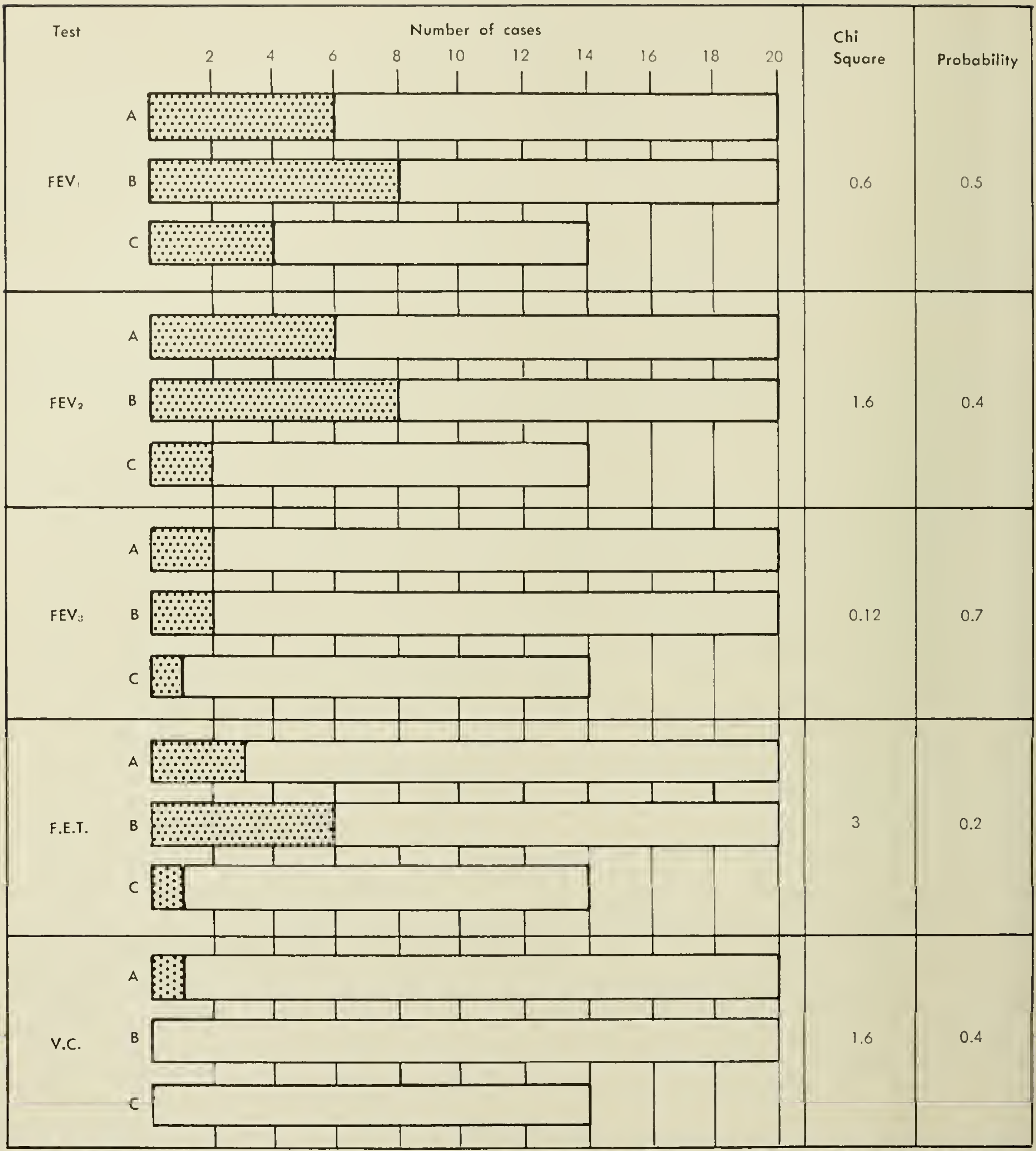

Fig. 1. Comparative frequency of incidence of significant changes in V.C. and T.V.C. (FEV$_1$, FEV$_2$, FEV$_3$, and F.E.T.) after subcutaneous administration of epinephrine under 3 different conditions: (A) before treatment, (B) under Ismelin®, and (C) under Ecolid®. The shaded area represents number of cases showing significant change in particular test after epinephrine.

Application of the chi square test to the results showed no significant difference so far as the T.V.C. or the V.C. are concerned (Fig. 1), yet as to the M.B.C., the A.V.I., and the battery of all tests, a statistically significant higher number of cases showed significant change after epinephrine under treatment with Ismelin®, as compared with the number of cases showing a similar change before treatment, (Table 2 and Fig. 2). The difference between the number of cases showing significant change in the different pulmonary function tests after epinephrine and before treatment—as compared with the number of cases showing a similar change under treatment with Ecolid®—was found to be insignificant.

From the data it is evident that 8 patients, who

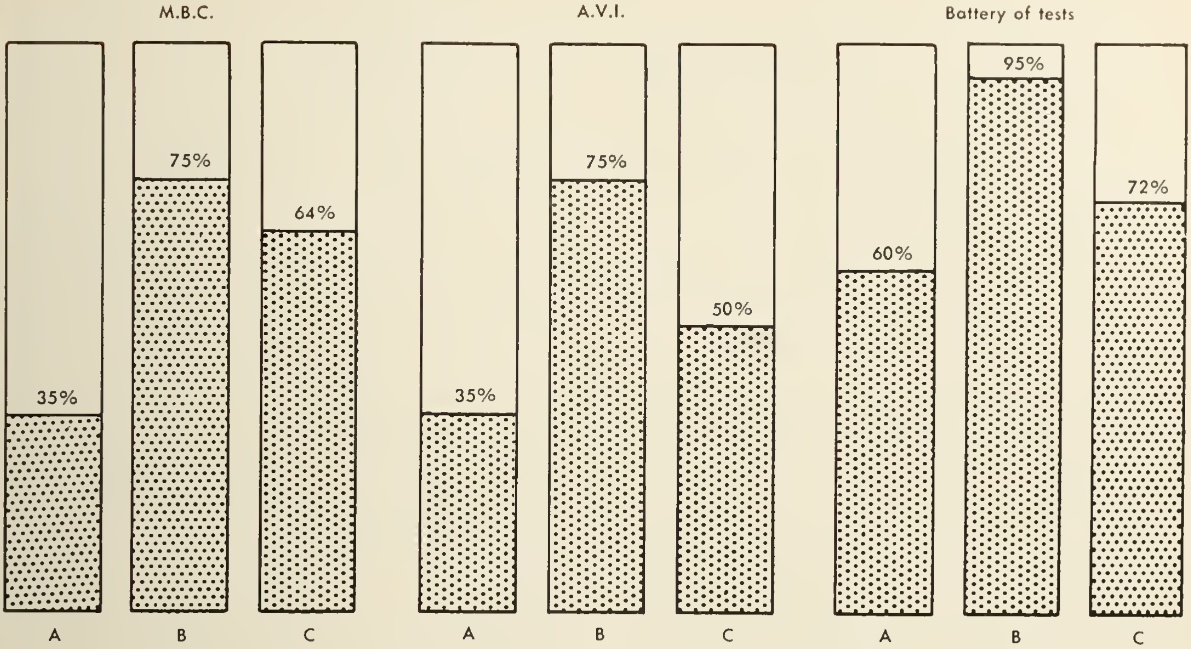

Fig. 2. Comparative frequency of occurrence of significant change after epinephrine. Each column represents total number of cases studied expressed as 100%, which for A and B is 20 cases and for C is 14 cases. The shaded area in each column represents percentage of cases showing significant change in particular pulmonary function test after the subcutaneous administration of epinephrine. (A) Before treatment, (B) under treatment with Ismelin®, and (C) under treatment with Ecolid®

did not show any significant increase in their M.B.C. or A.V.I. following the subcutaneous administration of epinephrine, recovered their responsiveness to the bronchodilator effect of epinephrine after a one-week treatment with Ismelin®. These actually constitute 61.5% of the 13 patients who were previously epinephrine-fast. Similarly, 7 patients, who did not show any significant change in any of the tests following epinephrine administration, recovered their responsiveness to the bronchodilator effect of the drug under treatment with Ismelin®. These patients actually constitute 88% of the previously 8 epinephrine-fast, nonresponsive cases.

SIDE EFFECTS AND COMPLICATIONS

Under treatment with Ismelin®, 2 patients, or 10%, developed mild diarrhea on the third and fourth days of treatment, which disappeared spontaneously on the continuation of therapy. Transient muscular weakness was observed in 2 patients, or 10%, and slight postural hypotension in 3 patients, or 15%. In no patient was it necessary to discontinue the drug because of side effects.

Under treatment with the ganglion blocker, Ecolid®, on the other hand, 6 patients, or 30%, developed postural hypotension. In 4 of these patients the postural hypotension was severe and necessitated stopping treatment. Also 2 patients developed fever and pneumonitis, which necessitated discontinuation of treatment. Thus, 6 patients could not continue therapy because of side effects. Slight blurring of vision and constipation developed in 4 patients.

DISCUSSION

The degree of increase in the FEV_3 after epinephrine in patients under Ismelin® is about double the increase in these patients before treatment.

Eight cases were shown to be epinephrine-fast. They failed to show significant change in any of the pulmonary function tests. Under treatment with Ismelin®, 7 out of these 8 cases, or 88%, recovered responsiveness to epinephrine and showed bronchodilatation according to results of the battery of pulmonary function tests.

Application of the chi square test to the number of cases showing significant change after epinephrine in the different pulmonary function tests, before and under treatment with Ismelin®, shows a statistically significant difference in favor of Ismelin® treatment in the M.B.C. and A.V.I. tests and in the whole battery of tests (Fig. 2).

The comparison between Ismelin® and the ganglion blocker Ecolid® showed the superiority of Ismelin®.

Although a difference was shown in the mean change in the different pulmonary function tests used in the patients before treatment and under treatment with Ecolid®, none of the applied tests showed a statistically significant difference when studied with Student's T-test. This was in contrast with the findings under treatment with Ismelin® in relation to the FEV_3.

Although there was a difference in the frequency of significant changes in the different pulmonary function tests used before and during treatment with Ecolid®, the difference, tested with the chi square test, was statistically insignificant. This was in contrast with the significant differences detected with Ismelin® in the M.B.C. and A.V.I. tests and the whole battery of tests used.

Side effects were more common with Ecolid® than with Ismelin® and 6 patients had to discontinue use of Ecolid®. No patient had to stop Ismelin® because of side effects.

This superiority of Ismelin® in potentiating the bronchodilator effect of epinephrine may be related to the different site of action. According to the law of denervation, the degree of hypersensitivity of smooth muscle is greater if the postganglionic nerves are interrupted, as with Ismelin®, than if the ganglia are blocked as with Ecolid®.

SUMMARY AND CONCLUSIONS

The present study demonstrates the value of Ismelin® as a potentiator of the bronchodilator effect of epinephrine in 20 selected cases of chronic bronchial asthma. The mean increase in the FEV_3 after epinephrine, during treatment with the drug, doubles. It was also shown that 88% of the epinephrine-fast cases recovered their responsiveness to epinephrine under treatment with Ismelin®. It was found to be superior to the ganglion blocker, Ecolid®, in this respect and with lesser incidence of side effects.

It is suggested that Ismelin® may be applied to prevent or retard the development of progressive resistance in the chronic asthmatic patient to epinephrine or related drugs and to enhance his response to these bronchodilators.

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Vascular Hamartoma of the Lung

B. N. VARMA, M.B., B.S., T.D.D.
Birmingham, England

Among the congenital vascular tumors of the lung, vascular hamartoma is a relatively uncommon condition. There are few authentic cases in literature. Albrecht was first to describe this condition and the word "hamartoma" was coined by him in 1904. Hamartoma, in general, designates a tumor-like formation consisting of abnormal mixture of histological components normally encountered in an organ. The following is the report of a proved case of vascular hamartoma.

CASE REPORT

A 35-year-old laborer was first seen on May 21, 1963, for what he called "off-color" (malaise) and progressive exertional dyspnoea during the past eight months. At the time of examination he had dyspnoea grade I. On direct questioning he revealed that he coughed up small quantities of fresh blood on occasions during this interval of his illness. He was a moderate drinker of alcohol and smoked an average of 40 cigarettes per day for several years. He had rheumatic fever at the age of 10. On closer questioning it was noted that his father had marked clubbing of the fingers, although he was unable to recollect whether there was cyanosis of the skin and mucous membrane. The patient has 3 living children and all are well.

On examination he was found to be in good general condition. There was central cyanosis which was exaggerated on physical exertion. There were several capillary telangiectases on the lower lip, each measuring about 1 to 2 mm., and fading on pressure. He had marked clubbing of the fingers and toes (Figs. 1 and 2). His cardiovascular system showed no abnormality. Blood pressure was 120/80 mm. Hg. On examination of his chest, a systolic bruit was heard over the right inframammary region, and a similar but separate murmur was heard over the left infraclavicular region. The murmurs had no relation to the cardiac cycle and were sharply accentuated during inspiration. No abnormality was detected in the other systems clinically.

INVESTIGATIONS

1. *Blood*

Hemoglobin level varied between 18.9 gm. percent to 22 gm. percent.
Red cells 7,500,000 per cubic millimeters
Erythrocyte sedimentation rate, less than 1 mm. per 1st hour (Wintrobe)
Packed volume cells 60%
Mean corpuscular hemoglobin concentration 35%
Platelets 375,000 per cubic millimeters
White blood count 6,200 per cubic millimeters
Polymorphs = 48%
Lymphocytes = 44%
Monocytes = 7%
Eosinophils = 1%

Bone Marrow Studies

Neutrophils	32 %
Neutrophil metamyelocytes	24 %
Neutrophil myelocytes	12 %
Eosinophils	1.5%
Eosinophil metamyelocytes	1.5%
Promyelocytes	1.5%
Myeloblasts	0.4%
Megakaryocytes	0.4%
Haemocytoblasts	0.4%
Proerythroblasts	0.4%
Early normoblasts	1.5%
Intermediate normoblasts	8.0%
Late normoblasts	5.5%
Lymphocytes	5.0%
Plasma cells	1.1%
Reticulum cells	1.1%

MYELOID/ERYTHROID (ratio 5 to 1)

2. *Blood Volume and Cardiac Output*

Cardiac output — 6.5 and 6.6 l. per minute (two readings isotopic method)
Plasma volume — 2.9 l.
Blood volume — 5.9 l.
Pulmonary blood volume — 440 ml.

3. *Circulation*

Pulmonary circulation time — 4.5 sec.
Arm to right ventricle time — 10 sec.

4. *Electrocardiograph*

Within normal limits

B. N. VARMA *is registrar, East Birmingham Hospital (Chest Branch), Birmingham.*

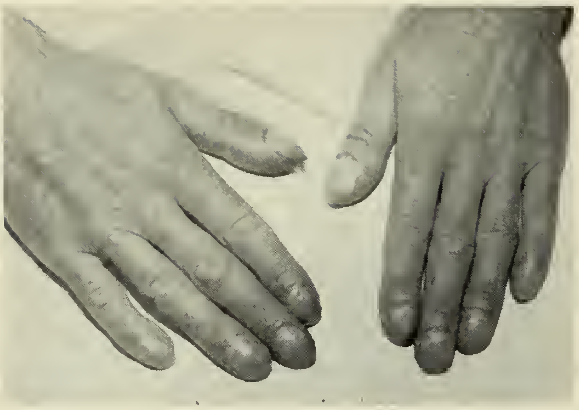

Fig. 1. Showing clubbing of hands

5. *Cardiac catheterization*

	Pressure			*Blood gas volume percent*		
Position	*Systolic*	*Diastolic*	*Mean*	*02 Capacity*	*Content*	*Percent saturation*
Pulmonary artery	10	2	5	25.3	17.2	68
Brachial artery					21.5	85
Right ventricle	15	0				
Right atrium			−2			

Oxygen consumption 266 ml. per minute
A-V O_2 Diff. 4.3 vols. percent
Cardiac output – 6.2 l. per minute (Ficks principle)

6. *Blood*

pH 7.33
PCO_2 45 mm. Hg.
Bicarbonite – 21.5 mEq.

7. *Chest X-ray (Fig. 3)*

Two radio translucent areas each measuring 2 cm. × 2 cm. over right lower zone and left midzone.

8. *Tomography (Fig. 4)*

Right side: In lower zone a translucent area running toward hilum
Left side: (Fig. 5) In midzone a translucent area running toward hilum

9. *Pulmonary angiocardiograph (Fig. 6)*

Homogenous radio-opaque areas filled with dye by large feeding vessels and also larger sizes of veins draining back into left atrium.

10. *Pulmonary function tests*

Vital capacity (V.C.) – 4.3 l. per minute
Force expiratory volume (F.E.V_1) – 2.95 l. per minute
Expiratory flow rate – 420 l. per minute

11. *Sputum*

Negative for tubercle bacilli on several occasions and on culture also.

A preoperative diagnosis of bilateral pulmonary arteriovenous communications involving the right lower lobe, left upper lobe, and secondary polycythaemia was made.

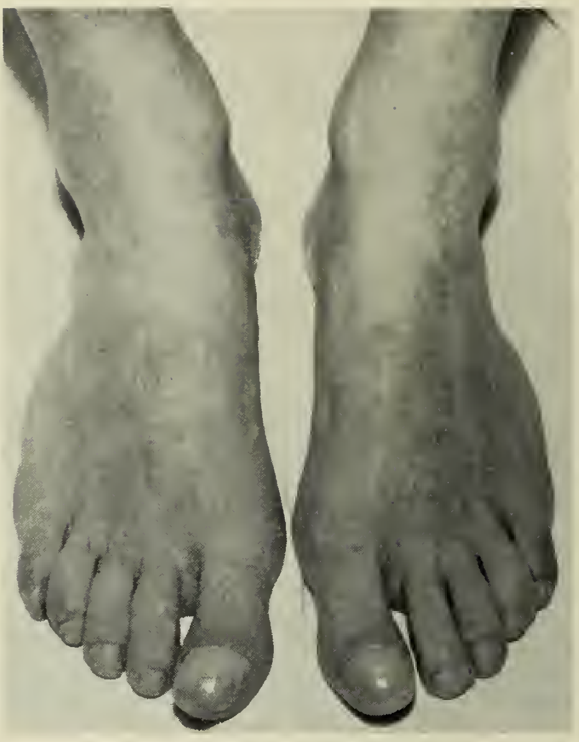

Fig. 2. Showing clubbing of feet

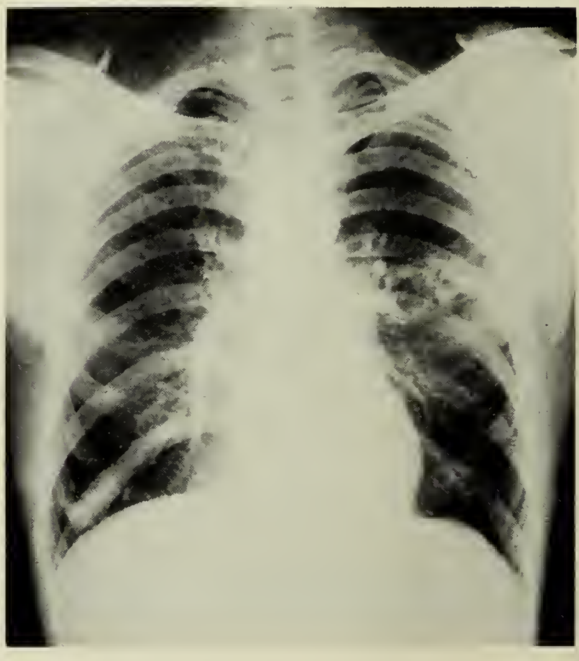

Fig. 3. Chest X-ray showing radiotranslucent areas in right lower and left midzones

TREATMENT

On July 7, 1963, the right lung was exposed by right sided thoracotomy through the bed of the sixth intercostal space under general anaesthesia. The right anterior basal segment was resected including the tumor.

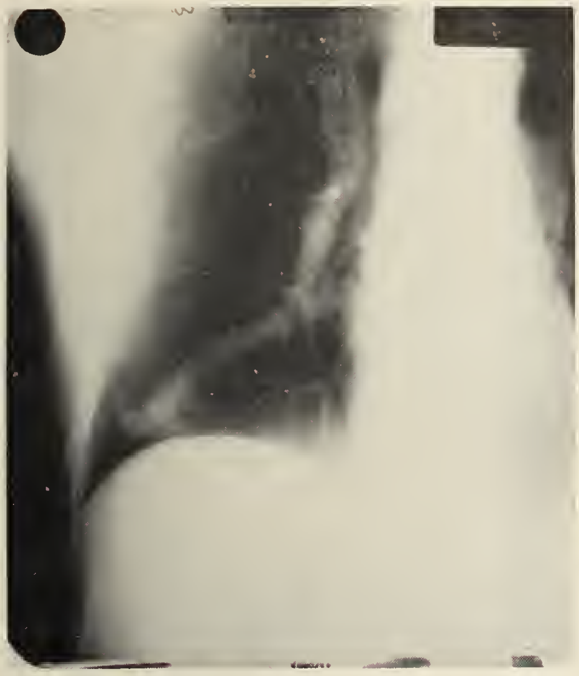

Fig. 4. Right sided tomograms showing radiotranslucent area in lower zone running towards hilum

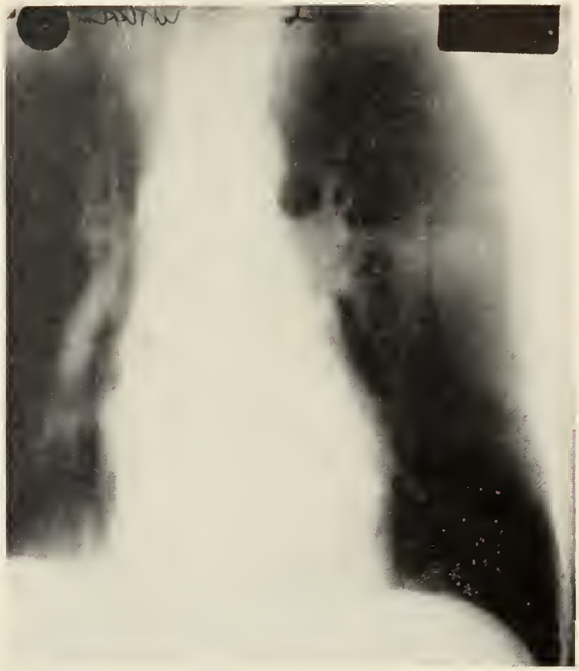

Fig. 5. Left sided tomograms showing radiotranslucent area in midzone running towards hilum

PATHOLOGICAL REPORT

The resected segment (Fig. 7) showed a ragged piece of lung 7 × 4 × 3 cm. On the raw surface there were 2 open cavities each about 0.5 cm. in diameter and these were probably vessels. No further definite abnormal vessels were found.

Microscopic examination. Throughout the specimen there was an excess of small blood vessels with abnormal walls. Sometimes these were thick and cellular, hyaline, and partly occluded by irregular intimal thickening, possibly organized mural thrombus. In addition, there were occasional larger and almost cavernous vessels with disorganized fibromuscular walls (Fig. 8). The picture is consistent with the diagnosis of vascular hamartoma of the lung.

POSTOPERATIVE PROGRESS

During the postoperative period the patient felt remarkably well and exertional dyspnoea was alleviated. Cyanosis improved, the continuous murmur over the right side of the chest disappeared, and the hemoglobin level fell to 15.6 gm. percent (Fig. 9) on the tenth day of the postoperative period. He was discharged on Aug. 3, 1963.

Unfortunately, the patient was reluctant to undergo repeat investigations or any more surgical intervention for the left sided lesion. He did not appear for follow-up.

DISCUSSION

Vascular hamartoma is a pathological diagnosis. Usually they are poorly demarcated and show intimate mingling of superfluous vessels with the normal tissue of the organ in which they are contained.

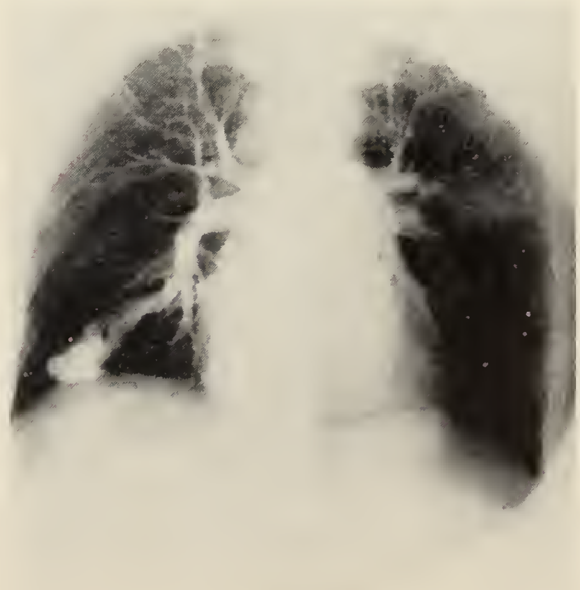

Fig. 6. Pulmonary angiocardiograph showing radio-opaque areas filled with dye by large feeding vessels and veins draining back into left atrium

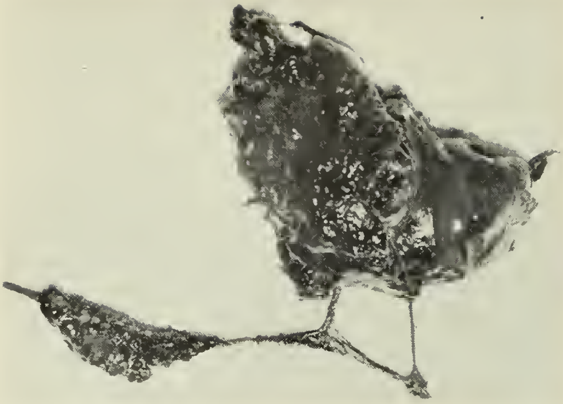

Fig. 7. Resected specimen of right anterior basal segment including tumor

The clinical picture depends on the degree of arteriovenous shunt. Central cyanosis, early clubbing, and secondary polycythaemia are the presenting features of the disease. Exertional dyspnoea and syncopal attacks are the main symptoms that may bring the patient to the doctor. On the other hand, the case may be asymptomatic, the discovery being accidental. The presence of a continuous bruit over the site of the tumor and the characteristic radiological findings confirm the arteriovenous communication. The condition may be mistaken for the other congenital and acquired cyanotic diseases of the heart and lungs.

The present case presented with a short history of malaise and exertional dyspnoea. He had central cyanosis, clubbing of the digits, and continuous murmurs over the right lower and left upper zones. Detailed investigations showed secondary polycythaemia, increased pulmonary circulation time, a slightly raised cardiac output, and normal physiological cardiac pressures. Arterial oxygen saturation was 85%. The chest X-ray was suggestive, and angiocardiography confirmed the presence of vascular lesions in the lungs. In view of his progressive physical disability and the fear of complications, such as vascular thrombosis and unexpected but sometimes fatal haemoptysis, he was subjected to immediate surgery. The right anterior basal segment, including the hamartoma, was resected. Postoperatively he made an excellent recovery both subjectively and objectively. Unfortunately, the patient refused a second operation for his left sided lesion and still remains under the potential dangers and complications of the disease.

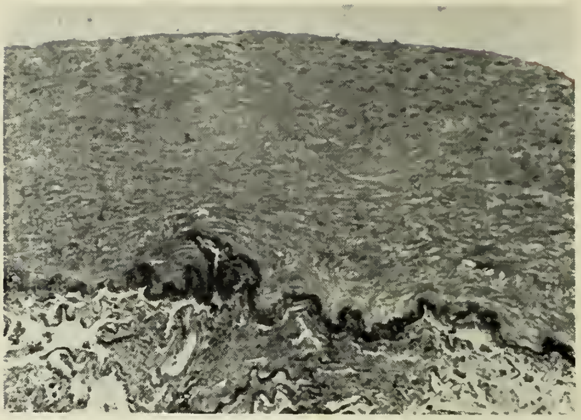

Fig. 8. Showing microscopic picture

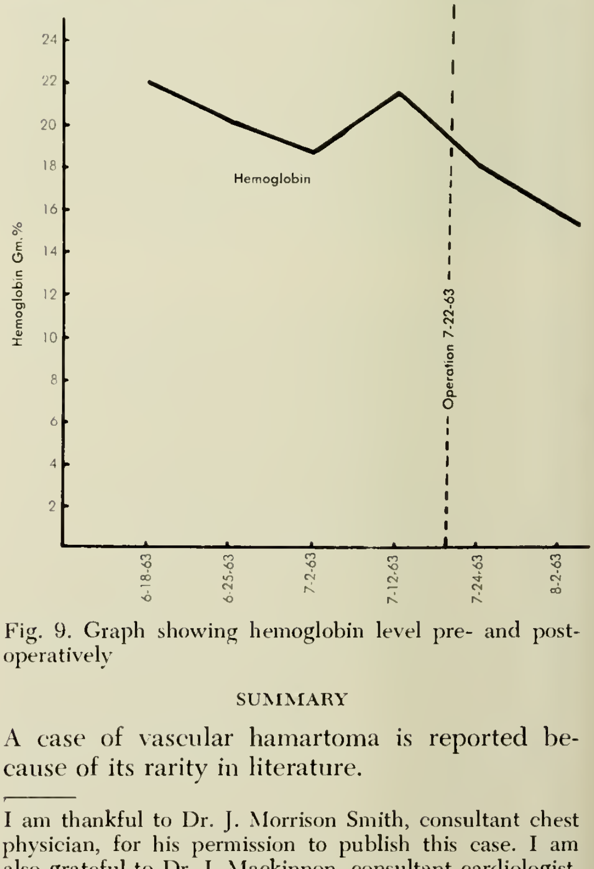

Fig. 9. Graph showing hemoglobin level pre- and postoperatively

SUMMARY

A case of vascular hamartoma is reported because of its rarity in literature.

I am thankful to Dr. J. Morrison Smith, consultant chest physician, for his permission to publish this case. I am also grateful to Dr. J. Mackinnon, consultant cardiologist, Mr. S. F. Stephenson, consultant thoracic surgeon, and Dr. R. G. F. Parker, consultant pathologist, for their help. My thanks are also due to our secretaries, Miss J. A. Goodwin and Mrs. B. J. Tennant. I extend my sincere thanks to my friend Dr. V. Parmeshwara for his criticism.

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JAMES J. WARING *Series*

Prescalene Lymph Node Biopsy

CHARLES HARVEY, M.D., and J. L. ALEXANDER, M.D.
Tallahassee, Florida, and Savannah, Georgia

IN 1949, Daniels reported the diagnostic value of study of the prescalene lymph nodes in pulmonary disease. Subsequently, a number of reports of the use of this procedure have been published both in American and foreign literature. Since medical library facilities are limited in this city, a complete review of the literature for this paper is not feasible. For this reason, no specific citations are included in this article. Omission of the citation of any specific reference is not intended to imply that the authors feel that this reference is not valuable but simply that this reference is not available to us.

A review of the American literature available to us shows that 886 prescalene lymph node biopsies are reported, of which 30.8% proved diagnostic. In these various series, positive diagnoses range from a low of 12% to a high of 40%. From this literature, several impressions can be gained. [1] Prescalene lymph node biopsy is most likely to be of value in the presence of mediastinal lymphadenopathy and in diffuse pulmonary granulomatous processes. [2] Prescalene lymph node biopsy is of questionable value in pulmonary malignancy, unless supraclavicular lymph nodes are actually palpable. [3] Prescalene lymph node biopsy is probably of no value in diffuse, nongranulomatous pulmonary processes.

The majority of reported series of prescalene lymph node biopsy have originated, not surprisingly, from centers devoted to the diagnosis and treatment of chest disease. This means, by inference at least, that the patients concerned in these reports have been rather thoroughly prescreened and that most, if not all, of the more common diagnostic modalities have been exhausted before prescalene lymph node biopsy. In contradistinction to these series, this series of cases comes from admissions to the service of a metropolitan general hospital, and little or no prescreening has taken place.

As one analyzes the literature, it becomes obvious that the percentage of positive diagnoses established by prescalene lymph node biopsy diminishes in direct proportion to the frequency with which this procedure is used. If the cases are carefully selected to include only those cases with parenchymal and mediastinal involvement, it seems obvious that the diagnostic batting average for this procedure will be quite high. If, on the other hand, prescalene lymph node biopsy is done as a routine procedure in all cases of pulmonary disease which defy diagnosis by the commoner means of history and physical examination, routine X-rays, bronchoscopy, and sputum examination for bacteriology and cytology, then, of necessity, the diagnostic batting average will decline. We do not feel that this fact is grounds for condemnation of the procedure, since any diagnostic procedure which yields an incidence of positive diagnoses approaching 100% is probably not being used often enough.

MATERIAL

The cases included in this report comprise 100 patients, seen by the chest service of a general hospital in this municipality. Criteria for selection of patients were loosely applied and can be simply stated. Obviously, pulmonary, pleural, or mediastinal disease or some combination of these three was present. The diagnosis remained obscure after historical data had been obtained, physical examination done, appropriate X-ray studies obtained, bronchoscopy carried out, and sputum bacteriology or cytology, or both, had been done. In many cases, the correct diagnosis was at least strongly suspected before being finally confirmed, but in no case was the diagnosis proved before prescalene lymph node biopsy. In many cases, as a glance at the accompanying charts will show, neither was the diag-

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CHARLES HARVEY *and* J. L. ALEXANDER *are from the Department of Surgery, Section on Thoracic Surgery, Memorial Hospital of Chatham County, Savannah, Georgia. Dr. Harvey's present address is Tallahassee, Florida.*

nosis confirmed following prescalene lymph node biopsy (Tables 1 through 5). Depending upon our clinical impression as to the importance of establishing a tissue diagnosis in these patients, some patients remain without confirmed diagnosis. In some patients, a final diagnosis was established by means of lung biopsy or by formal thoracotomy, and in a distressing number of cases, a final diagnosis was established at autopsy.

TABLE 1

RESULTS OF LYMPH NODE BIOPSY

Final diagnosis	*Scalene positive*	*Scalene negative*
Bronchogenic carcinoma	19	5
Bronchogenic carcinoma (not proved)		13
Cancer metastatic to lung	2	3
Sarcoidosis	13	9
Tuberculosis	7	3
Multiple myeloma		2
Ependymoma metastatic to lung		1
Pulmonary fibrosis		1
Lymphoma	3	1
Chronic interstitial pneumonia		1
Silicosis		2
Lung Abscess		2
Mediastinal tumor		1
Undiagnosed pulmonary lesion		2
Unresolved pneumonia		1
Pulmonary actinomycosis		1
Pleural effusion postpneumonic		1
Carcinoma metastatic to mediastinum		1
Bronchiectasis		1
Lymphoma (not proved)		1
Malignant melanoma metastatic to lung		1
Hilar lymphadenitis	1	
Fibrosarcoma of chest wall		1
Neurolemmoma of mediastinum		1
Totals	45	55

TECHNIQUE

The prescalene lymph node biopsies here reported were carried out either by a member of the attending staff or by various members of the surgical resident staff at the first-, second-, and third-year levels. Since all cases included in this report were on the service of the senior author, a certain standardization of operative technique was possible. The operative technique used is simple and straightforward, and emphasis is placed upon a careful, meticulous excision of the prescalene fat pad, with its contained lymph nodes, from a level just above the point where the omohyoid muscle crosses the prescalene fat pad, down to the insertion of the anterior scalene muscle on the first rib, the area being bounded medially by the internal jugular vein, posteriorly by the anterior scalene muscle, anteriorly by the sternocleidomastoid muscle, and laterally by the external jugular vein. It is probably worthwhile to note parenthetically that, in the course of dissection such as this, one tends to follow the path of least resistance, and a valuable addition to the operative team is an assistant who will continually remind the operator that the major focus of the dissection should be inferomedial rather than inferolateral. We feel that, unless the nodes which lie just posterior to the angulus venosus are removed, an incomplete dissection has been done. We feel that it is also important to stress the fact that this is a dissection in an area where many important structures are present, vulnerable, and hidden. Good light and adequate assistance are imperative. This is not a procedure to be carried out hurriedly, in the interim between major surgical procedures. Emphasis must be placed upon a careful and meticulous dissection, done in an unhurried fashion, else its diagnostic accuracy is impaired and the potential for annoying, if not disastrous, complications is real.

The patient is positioned on the operating table in a comfortable semisitting position, with the head rotated away from the operative side and the neck extended. Since the average operating time for this procedure is between twenty and forty minutes, it is of some importance that the patient be made as comfortable as possible. In very few cases have we found it necessary to place a bolster underneath the shoulders of the patient, in order to extend the neck adequately, and we have found that abandonment of this particular item in positioning of the patient adds a great deal to the comfort of the patient himself. In general, we have found that by simply lowering the head piece of the operating table slightly the neck can be adequately extended. The proposed operative field is prepared in a manner satisfactory to the current whim of the operating surgeon and is draped. Drapes are held off the patient's face by an appropriately placed Mayo stand, this, too, adding considerably to the comfort of the patient. The proposed site of operation is thoroughly infiltrated with a solution of lidocaine (Xylocaine®) and epinephrine (Adrenalin®), following which the operation proper is begun. The incision is placed approximately 2½ fingerbreadths above the point at which the sternocleidomastoid muscle joins the clavicle, paralleling a natural flexion crease in the neck. Approximately one-third of the incision overlies the body of the sternocleidomastoid muscle, and two-thirds of the incision lies lateral to this muscle. A generous incision is made. The incision is carried down through the platysma muscle, and the lateral margin of the sternocleidomastoid muscle is freed both superiorly and inferiorly. We have found that this simple maneuver tremendously increases our operative exposure. The body of the sternocleidomastoid muscle itself is then infiltrated with 5 to 10 cc. of Xylocaine® solution. The dissection is carried directly down to the anterior scalene muscle, and the phrenic nerve is identified coursing across the anterior body of this muscle. An attempt is made to avoid incising the fascia covering the anterior scalene muscle. The omohyoid muscle is then identified, usually at the lower margin of the skin incision, and the dissection carried beneath it. The internal jugular vein is next identified. With all major landmarks thus identified, the prescalene fat pad, with its contained lymph nodes, is then excised, great care being taken to insure that the anterior body of the scalene muscle and the internal jugular vein are thoroughly cleaned of all fatty and lymphoid tissue. In the elderly patient, the rather tortuous transverse cervical artery and vein lie well within the substance of the prescalene fat pad, and considerable care in dissection must be exercised in order that these structures not be injured. Bleeding from a severed transverse cervical artery, deep in a fatty neck, renders this a somewhat messy procedure. At the inferior extremity of the dissection, again, considerable care must be exercised, since the angulus venosus is both vulnerable and hidden. On the left side, care must be taken to avoid injury to the thoracic duct: a precaution, it may be said, which is not always successful in attaining its objective. If the thoracic duct is severed, this fact becomes immediately obvious by the accumulation of significant and annoying amounts of chyle in the operative wound. A thorough search is made for the point of leak, which is ligated with No. 4-0 black silk. Chylous drainage has not been a problem postoperatively. After the dissection has been completed, the patient is instructed to cough vigorously 2 or 3 times, on the theory that if bleeding is to occur as the result of coughing and the resultant increase of venous pressure blowing off a tie or dislodging a clot in a small vessel we want it to occur at this time, rather than after the patient has been returned to his room. The wisdom of this precaution has been demonstrated on several occasions, since, occasionally, a vigorous cough will be followed very shortly by vigorous bleeding. After the surgeon has determined to his satisfaction that no significant lymphatic or hemic leak exists, the wound is closed in 2 layers. Early in the series, these wounds were routinely drained with a small Penrose wick. Latterly, drainage has not been a routine procedure. We have been unable to ascertain any real effect on wound healing from drainage or the omission thereof. The platysma muscle is closed with interrupted sutures of fine catgut, and the skin is closed with interrupted sutures of No. 4-0 black silk.

Emphasis has already been placed upon the necessity for a careful, thorough dissection of the node bearing prescalene region. At least as important is a thorough examination of a resulting specimen by the pathologist. The histopathological diagnoses recorded herein are the results of study of each individual specimen by one of five pathologists, all of whom make a point of careful examination of the fat pad, careful dissection of all contained nodes, and study of multiple sections of each node. If the nodes contained in the specimen be tiny, the entire specimen is embedded, and multiple sections are studied.

RESULTS

This report encompasses 100 patients upon whom prescalene lymph node biopsies were done.

TABLE 2

RESULTS OF LYMPH NODE BIOPSIES

Reticuloendothelial hyperplasia	28
Carcinoma	21
Normal nodes	17
Sarcoid	13
Lymphadenitis	7
Tuberculosis	3
Hodgkin's disease	3
Granuloma	2
Giant-cell granuloma	2
Congestion of nodes	1
No nodes	3
Total	100

It will be noted that reticuloendothelial hyperplasia was reported in 28%, carcinoma in 21%, and sarcoidosis in 13%. Tuberculosis was diagnosed in only 3% of our cases of prescalene lymph node biopsy. As much as anything else, this probably reflects the fact that this procedure is seldom used when tuberculosis is strongly suspected, since a large number of cases of tuberculosis are diagnosed in our clinics each year. The 2 cases reported as granuloma and the 2 reported as giant-cell granuloma probably represent tuberculous nodes; however, the pathologist who read these slides is loath to make a diagnosis of tuberculosis in the absence of demonstrated acid-fast bacilli. Seventeen percent of the procedures done resulted in finding nodes that were histologically normal. In the remaining 15% of cases, the diagnoses are distributed among a variety of conditions, ranging from lymphadenitis (7%) through Hodgkin's disease (3%) and congestion (1%); no nodes in the specimen accounted for 3%. We feel it is worthy of mention that it was found, upon investigation, that in each of the instances in which no nodes were found, the procedure was done by a resident early in the course of his training. We reject the concept of congenital absence of scalene nodes, believing that the absence of nodes in the specimen reflects incomplete dissection, rather than absence of prescalene lymph nodes. In each of these three instances, the error was pointed out to the involved resident, and subsequent dissections by this individual always yielded nodes in the specimen.

CARCINOMA

We were interested to find just how useful this procedure might be in the determination of extrathoracic metastasis in cases of carcinoma, in the absence of palpable nodes. Prior articles on this subject have indicated that the incidence of positivity was quite low if supraclavicular nodes were not palpable, so low, in fact, that the procedure is of doubtful value under these conditions. We found that of 12 cases eventually proved to be bronchogenic carcinoma and who had palpable supraclavicular nodes 10 cases, or 85%, yielded a definite diagnosis. Of 25 cases, eventually proved to be bronchogenic carcinoma, in whom no supraclavicular nodes were palpable, 11, or 44%, yielded a positive diagnosis.

TABLE 3

INCIDENCE OF PALPABLE NODES

	Positive nodes	*Negative nodes*	*Totals*
Nodes palpable	10	2	12
No nodes palpable	11	14	25

Admittedly, this is a small group of cases, but it would seem that an incidence of 44% of positivity would warrant the inclusion of this procedure in the diagnostic armamentarium in cases where the diagnosis of carcinoma is suspected but not proved. Also worthy of note is the fact that, in the great majority of cases of positive nodes, the tumor was located centrally, although in such a position that it could not be demonstrated via the bronchoscope. We have formed yet another clinical impression from our experience of removal of prescalene lymph nodes containing metastatic tumor. In the majority of cases of prescalene lymph node biopsy in which malignancy is not a consideration, cleavage planes are easy to develop, and the dissection of the fat pad is attended by little or no bleeding. However, in cases where the nodes contain metastatic deposits—even microscopic metastases—cleavage planes are difficult to develop, and the dissection is hampered by a great deal of troublesome oozing. No ready explanation for this fact is offered but we suspect it relates to impairment of blood and lymph flow through nodes partially replaced by metastatic tumor.

SARCOIDOSIS

Twenty-five patients were diagnosed on clinical grounds as having Boeck's sarcoid. Of these, in 13, or 50%, a histopathologic diagnosis of sarcoid was established by prescalene lymph node biopsy.

TABLE 4

RESULTS OF LYMPH NODE BIOPSY

Hyperplasia	5
Sarcoid	13
Normal	7
No nodes	1
Total	26

This incidence was disappointingly low. In all cases of mediastinal adenopathy, with enlargement of the right paratracheal node, the biopsy was diagnostic. In the 12 cases in which the biopsy was not diagnostic, the true diagnosis remains in doubt, since, for a variety of reasons, no more extensive biopsy procedures (lung or mediastinal) have been carried out.

TUBERCULOSIS

As previously stated, this procedure was seldom used when tuberculosis was the disease of major consideration, since, except in the case of minimal or miliary disease, the diagnosis can usually be made by the use of sputum smears and cultures. The fact that, in this series, tuberculosis was definitely diagnosed on 3 occasions and presumptively diagnosed on 4 other occasions, makes one wonder if this might not be a more rapid method of establishing this diagnosis than is the sputum culture. Of these 7 cases, one was thought initially to have tuberculosis on the basis of a localized pulmonary lesion. Three presented with a primary pleural effusion, while one was thought initially to have bronchogenic carcinoma and one a mediastinal lymphoma. A series of scalene node biopsies in patients with proved pulmonary tuberculosis will be the subject of a later report.

COMPLICATIONS

Four significant complications arose as a result of prescalene lymph node biopsy. One patient developed a wound infection from which staphylococcus was recovered. This infection responded to reopening of the wound and antibiotic therapy with penicillin. No permanent damage, other than an unsightly scar, resulted. In 2 cases, postoperative bleeding was a problem. In one of these patients, bleeding was probably secondary to thrombocytopenia, which was, in turn, a reflection of hyperspleenism. In the second case in which bleeding was a complication, an artery in the depths of the wound bled several hours after the biopsy procedure had been carried out, presumably because of a dislodged ligature. This required reopening of the wound and religation of the vessel. In one patient, an extensive skin slough resulted, when the syringe used for local anesthesia was filled with 70% alcohol, rather than Xylocaine® solution. These complications represent a 4% incidence of significant complications, directly attributable to the biopsy procedure.

SUMMARY AND CONCLUSION

One hundred consecutive prescalene lymph node biopsies, from the services of a general community hospital, have been presented. The only patient selection involved relates to the impossibility of establishing diagnosis by conventional methods of history and physical examination, bronchoscopic examination, sputum bacteriologic and cytologic examination, routine chest X-rays, and bronchography. A wide variety of intrathoracic diseases was represented. Diagnosis was established by prescalene lymph node biopsy in 45% of the cases.

TABLE 5

RESULTS OF LYMPH NODE BIOPSIES

	Nodes (+)	*Nodes (−)*
28 Localized pulmonary lesions	10	18
31 Diffuse pulmonary lesions	14	17
47 Mediastinal involvements (X-ray)	23	24
13 Pleural effusions	8	5
Totals	55	64

A 4% significant complication rate resulted.

Emphasis is placed upon a meticulous and complete performance of the biopsy procedure and upon an equally meticulous and complete examination of the biopsy specimen by the pathologist.

This procedure has proved valuable in establishing a diagnosis in cases of bronchogenic carcinoma, both with and without palpable supraclavicular lymph nodes. It has likewise proved valuable, albeit less so, in establishing a diagnosis of sarcoidosis, although, in cases with hilar and mediastinal adenopathy, the percentage of positive diagnoses in sarcoidosis approaches 100. As a rather surprising sidelight, this procedure also proved quite valuable in establishing a diagnosis of intrathoracic tuberculosis, in which examination of the sputum and pleural fluids by direct smear was not diagnostic. Mediastinal lymphoma, although quite limited in this series from a numerical standpoint, proved readily diagnosable by this modality. In a variety of nongranulomatous and nonneoplastic pulmonary lesions, the procedure was worthless.

The Neuritic Patient

GEORGE C. FLORA, M.D., and A. B. BAKER, M.D.

Minneapolis

POLYNEURITIS or peripheral neuritis consists of a widespread involvement of the peripheral nerves which is usually bilateral and symmetrical, causing weakness and sensory disturbances in the hands and feet.

The clinical picture is the same, regardless of the cause and is characterized by deficit phenomenon of both the motor and sensory functions. There is usually early irritative sensory phenomenon which consists of hyperesthesias and dysesthesias of the hands and feet. These symptoms are usually followed by pain, which frequently is burning in nature. The sensory symptoms tend to spread proximally as the sensory defect develops, with decreased appreciation of pain, temperature, touch, and deep sensations.

Motor impairment is very common and first manifests itself distally and spreads proximally as weakness, hypotonia, areflexia, and atrophy. The degree of motor and sensory involvement varies from case to case with one deficit often predominating over the other.

Generally, the diagnosis of neuritis is easy, but the exact etiology is more difficult to evaluate. A specific knowledge of the onset of the disease and the age of the patient will frequently help diagnose the more common causes of this neurological disorder.

INFANCY AND CHILDHOOD

Acute onset. [1] *Diphtheria.* This is a familiar cause of acute neuritis in this age group. It is most frequent in the eight- and nine-year-old child but may be seen at any age. The peripheral nerves are frequently involved two to three weeks following the onset of the primary infection which characteristically first involves nerves to the soft palate and produces a speech disturbance and a tendency to regurgitate fluid through the nose. The polyneuritis spreads rapidly to affect the distal musculature as well as the proximal structures of the trunk and sphincters. The sensory complaints are those of peripheral hypesthesia and dysesthesia. This disorder is further characterized by extreme muscle tenderness and hyperalgesia.

Neurological examination shows muscle weakness of the palate. Intrinsic muscles of the pupil may be involved with subtle signs of dilation and slowed light response. Classical peripheral hypesthesia and hypalgesia of "stocking-glove" variety are seen. Strength is impaired in the distal as well as the proximal musculature and the sphincter tone of the bladder and bowel is weakened. The motor deficit is a lower motor neuron type with decreased tone, hyporeflexia, and atrophy.

The prognosis in diphtheritic neuritis is good. Recovery is usually complete within three months although in severely affected individuals it may require greater than two years for total recovery.

The treatment for this disorder is antitoxin administered intermuscularly early in the postinfectious period which prevents the involvement of the peripheral nerves. Antitoxin administered after the thirty-second day of the disease or later results in a frequency of nervous system involvement of 30 to 60%.

2] *Serum neuritis.* This disorder may follow administration of any serum preparation; however, tetanus and diphtheria are the most frequent offenders. The classical signs of peripheral neuritis or mononeuritis affecting the axillary, median, or radial nerves occur three to four days following an injection. Pain and muscle tenderness may persist for weeks to months.

The prognosis for total recovery is good; although delayed recovery for several months is not uncommon.

3] *Infectious mononucleosis.* This disease, which occurs mainly in children and young

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GEORGE C. FLORA *is with the Division of Neurology, University Hospital, Minneapolis, and* A. B. BAKER *is professor and director, Division of Neurology, University of Minnesota Medical School, Minneapolis.*

adults, is characterized by fever, adenitis, increased mononuclear blood cells, splenomegalia, and a subacute course. It is probably a viral infection, although no specific organism has yet been isolated. The clinical picture is that of a febrile illness, which is characterized by prominent adenitis and a pseudomembrane of the oral pharynx. In this disorder, a classical peripheral neuritis may be seen. The signs and symptoms have no specific characteristics. The neurological examination reveals hypesthesia and hypalgesia of "stocking-glove" type, associated with peripheral motor weakness, hypotonia, hyporeflexia, and atrophy. There is often quite severe muscle tenderness and radicular pain associated with the disease. The laboratory finding of increased heterophile antibody titer substantiates the diagnosis. The prognosis for this condition is guarded.

Treatment consists of bed rest, high parenteral and oral vitamin supplements of the B complex, vitamin C, vitamin B_{12}, and crude liver. If ascending paralysis develops, swallowing and respiration may be impaired, requiring respirator support. With bulbar involvement, the prognosis is guarded, and there is a high fatality rate from this otherwise benign infection when polyneuritis or a Guillain-Barré syndrome occurs.

4] *Lead intoxication.* This toxin is a cause of peripheral neuritis in this age group, but it rarely is seen in our midwestern area. Children are exposed by ingesting lead paint dust. This is seen along the east coast where leaded paint, which was applied to the houses years ago, is still present. Another source of lead in this age group is from the ingestion of paint from toys and cribs of old vintage which were decorated with paint containing lead. Other rare sources are water from lead-lined cisterns or water carried through old lead pipes.

The symptomatology consists of gastroenteritic crisis (colic), anemia, and confusional state associated with peripheral neuritis. The peripheral neuritis shows predilection for the radial nerves producing bilateral wristdrop. The neurological examination reveals a typical peripheral neuritis and frequently a "lead line" at the base of the teeth. Laboratory confirmation is aided by a moderately severe anemia with basophilic stippling of the red blood cells and by an increased urinary excretion of lead in a twenty-four-hour period.

Ethylenediaminetetracetic acid (EDTA) in doses of up to 1 gm. per 15 kg. of body weight daily for four to five days is therapeutic. Strict bed rest and both oral and parenteral administration of vitamins of the B complex, vitamin B_{12}, and ascorbic acid are recommended until recovery occurs.

Gradual onset. [1] *Nutritional deficiencies.* Peripheral neuritis in this age group is still seen due to nutritional deficiencies, primarily from food fads and from prolonged reducing diets. Severe malnutrition in this age group from such causes as chronic diarrhea, malabsorption syndrome, or starvation from anorexia nervosa occasionally produces a classical peripheral neuritis.

A typical polyneuritis is the presenting complaint. Occasionally, the picture of pellagra can be seen in those cases manifesting gastrointestinal symptomatology, glossitis, dermatitis of the exposed skin, mental changes or confusion, or combined system disease. In other cases, the classical picture of beriberi may be present with signs of cardiac involvement (tachycardia and congestive heart failure, peripheral edema) and extremely painful dysesthesias of the extremities.

The neurological examination in these cases reveals motor weakness which is greatest in the peripheral musculature, especially in the dorsiflexors of the feet and in the grip of the hand. Sensory testing reveals "stocking-glove" hypesthesia and hypalgesia.

The treatment for these cases of peripheral neuritis is prolonged bed rest with a well-balanced diet supplemented by oral ingestion of vitamins B and C. During the initial period of therapy, parenteral administration of thiamin chloride, vitamin B complex, vitamin B_{12}, and crude liver is indicated.

Prognosis for this disorder is favorable if rest and adequate vitamins are administered and further deficiencies prevented.

2] *Medications.* The gradual development of a typical polyneuritis is occasionally seen following the administration of a variety of medications, two of the more common offenders are penicillin and sulfadiazine. The clinical picture of the peripheral neuritis is in no way distinctive, manifesting as a slowly progressive painful peripheral sensory deficit associated with less prominent peripheral motor deficits.

The neurological examination is not distinctive. The diagnosis depends upon the awareness that these medications may cause the condition.

Treatment for this form of the disease is primarily one of bed rest associated with discontinuance of the medication. Supplemental vitamin therapy may be utilized. The prognosis for these conditions is very good.

ADULTS

Acute onset. [1] Guillain-Barré's syndrome is the most common cause for the sudden development of a peripheral neuritis in adult life. This condition is not a disease entity but a syndrome which probably has multiple etiologies. Clinically, this condition commences with severe radicular pain. This complaint frequently precedes the abrupt onset of a peripheral neuritis or other deficits by weeks and may be most widespread and difficult to control adequately. Concomitant with the onset of neuritis, which is frequently typically ascending in type, there is diffuse muscle tenderness greatest in the calf and thigh musculature.

Neurological examination shows the bilateral facial paresis which is quite pathognomonic. This finding associated with signs of "stocking-glove" hypesthesia and hypalgesia and motor weakness, more prominent in the shoulder and hip musculature than in the more peripheral muscles, often makes diagnosis fairly simple.

Treatment consists of absolute bed rest with adequate sedation until the muscle tenderness disappears. Passive movement of the involved limbs during immobilization is important to prevent contractures. A high intake of the water soluble vitamins in a balanced diet with oral supplements is a necessity. A high-protein diet should be given to prevent a negative nitrogen balance on these individuals.

The prognosis for the peripheral neuritis is favorable for complete return of function. When the Guillain-Barré syndrome progresses to involve more than the nerves, particularly the cord and brainstem, the prognosis becomes much less favorable.

2] *Toxins.* The heavy metals may precipitate the abrupt onset of a peripheral neuritis.

Excessive lead exposure is seen among individuals employed in the storage battery manufacturing plants and in individuals who reclaim lead from used storage batteries by burning the cases in poorly ventilated shacks. This intoxication is also seen in individuals who chronically absorb or ingest lead from exposure to leaded gasoline or from lead vapors or in the manufacturing of some glasses and chemicals.

Arsenical exposure is still common in individuals who frequently use arsenic-based insecticides, fruit sprays, and rodent poisons and in others who come in contact with arsenic containing paints, dyes, and chemicals. Homicidal and suicidal exposure is still one of the more popular seen in the practice of medicine.

Mercury exposure is seen in the farming population of this area where seed fungicides such as Ceresan are used. Industrially, mercury exposures occur in the manufacture of thermometers, X-ray machines, mirrors, and barometers. Mercury administration in the form of dermatologic ointments is still popular with some medical men. These heavy metals produce typical peripheral neuritis with relatively unique diagnostic clues. Lead neuropathy shows a marked predilection for the radial nerve. Consequently, these patients present themselves with the history of gastric colic and confusional states and show anemia with basophilic stippling, lead line along the gums, and bilateral wristdrop. Arsenical neuropathy frequently has a history of a severe gastrointestinal upset, a pemphigoid rash over the lower extremities, and a brownish keratosis of the palms. Mercury neuropathy usually has an encephalopathy with convulsions and a gross tremor of the hands.

Treatment for these neuropathies consists of bed rest with high-vitamin supplements and the appropriate medical agent. Dimercaprol (BAL) is useful for mercury and arsenical intoxications and ethylenediaminetetracetic acid (EDTA) is quite specific for lead poisoning.

Other toxins which may produce peripheral neuritis in this age group are the industrial solvents.

Exposure to trichloroethylene is common in industries where it is used as a solvent for fat, gums, and rubber and as a good degreaser.

The more familiar carbon tetrachloride also produces peripheral neuritis; exposure occurs in individuals who use or fill fire extinguishers, in those spraying with insecticides which are dissolved in this agent, or by some who work in plants where it is employed as a fat solvent or a dry cleaning agent.

Carbon disulfide is another prominent offender; it is also used as an industrial fat solvent and a vulcanizing agent and, extensively, in the manufacture of rubber and synthetics. These intoxications frequently have a prominent liver and cerebral manifestation and more often present as a confusional state which is self-limiting, only to be followed by a severe peripheral neuritis. The peripheral neuritis is not characteristic. The treatment does not differ from the previous general measures consisting chiefly of bed rest and vitamin therapy.

Prognosis for recovery of this peripheral neuritis is good, provided that continued exposure is prevented.

Gradual onset. [1] *Alcoholic neuritis.* One of the more common causes of neuritis in this age group is chronic alcoholism complicated by avitaminosis. Clinically, paresthesias, cramps in the calves, and severe leg pain over a period of days frequently developing during a period of abstinence are the presenting symptoms. The pain is most severe in the feet, especially the soles, and this is associated with a relatively characteristic hypersensitivity of the soles. The neurological examination reveals hypesthesia and hypalgesia of "stocking" distribution and associated bilateral partial foot drop. The skin of the lower extremities is characteristic and manifests moist redness, secondary fungus infections, brittle nails, and multiple sites of brownish pigmentation and bruises of the shins.

Physical examination often shows hepatomegalia, spider nevi of the shoulders and chest, and mental symptoms characterized by vociferousness and injudicious denial of obvious signs of disease.

Treatment consists of bed rest, high vitamin intake, and abstinence from further exposure.

The prognosis is always guarded because these patients seldom discontinue their drinking habits. Recovery from an initial involvement is good but becomes very slow when recurrences occur.

2] *Diabetic neuritis.* Diabetes mellitus most commonly presents as a mononeuritis multiplex but it also causes polyneuropathy. Gradual insidious onset with ill-defined vague pains and paresthesias of the lower extremities should alert the physician. Pain is the most common and constant complaint and it is described as "dull and aching" or rarely as "burning" of the feet. The condition may progress until the patient has some impairment of motor function but it is quite rare to be of gross proportion. Neurological examination reveals hypesthesia and hypalgesia of "stocking" type and, rarely, "glove" distribution. Motor testing may show mild weakness of the dorsiflexors of the feet with absence of Achilles tendon reflexes. The laboratory aids reveal elevated fasting blood sugar levels and abnormal glucose tolerance curves. Cerebrospinal fluid often has an elevated protein level to 100 mg. or more. Treatment consists of vigorous diabetic control during a period of absolute bed rest, often for longer than a month. Parenteral administration of thiamine, ascorbic acid, vitamin B_{12}, and crude liver is indicated until sensory symptoms become less painful and motor dysfunction shows improvement.

3] *Nutritional deficiencies.* The peripheral neuritis which is seen from these causes most often results from poor vitamin absorption due to gastrointestinal disturbances such as gastric carcinoma, malfunctioning gastroenteritic stoma, intestinal fistula, chronic diarrhea, prolonged vomiting, or chronic pancreatitis or from extended starvation and unwise dietary habits.

Chronic nutritional deficiencies produce typical polyneuritis in this age group.

Treatment is alleviation of the primary gastrointestinal abnormalities if possible and enforced bed rest, good diet and parenteral vitamins (B complex, B_{12}, C, and crude liver). Prognosis in these cases is dependent upon the primary disease but is often surprisingly good.

4] *Drug-induced neuritis.* Most drugs that have been used or are being used in the treatment of human ailments have caused peripheral neuritis in susceptible individuals. The more common drugs that cause peripheral neuritis are the barbiturates, the antibiotics (especially penicillin and sulfadiazine), and isoniazid. These medications and compounded ointments containing mercury and arsenic must always be remembered when one sees a case of polyneuritis.

5] *Systemic disease entities.* Most systemic diseases of degenerative or infectious type have been reported to produce peripheral neuritis; however, in practice, myxedema, polycythemia, porphyria, and the collagen diseases are the chief offenders. The peripheral neuritis which occurs is not unique.

Treatment of the primary disease along with bed rest and high-vitamin supplement will frequently produce improvement of the neuritis.

OLD AGE

Acute onset. [1] *Guillain-Barré syndrome.* The most common cause of the acute onset of peripheral neuritis at this age is this myriad of entities. The clinical picture, treatment, and prognosis have been given in the previous section.

Gradual onset. [1] *Alcoholic neuritis.* This again is the most common cause of neuritis of insidious onset. The clinical course, treatment, and prognosis were given in the previous section.

2] *Pernicious anemia.* Peripheral neuritis commonly marks the onset of this disease. The presenting symptomatology is most frequently one of a "tingling, numbness, crawling" sensation which develops in the fingers and toes. There is slow spread of the sensory disturbances to the more proximal parts of the extremities. Associated with the peripheral neuritis there is a classical, pale yellow discoloration of the skin, a bothersome glossitis, and the signs and symptoms of anemia. Neurological examination reveals a sensory deficit of "stocking-glove" type. Motor signs are characteristically absent in these cases, although decreased Achilles tendon reflexes are to be expected. Later, the classical posterolateral column degeneration is found.

The treatment for this disease should include vitamin B_{12} and crude liver (2 units per cubic centimeter injectable) to produce remission of the peripheral neuritis and to prevent the development of subacute combined degeneration. Therapy with vitamin B_{12} alone does not suffice to prevent cord damage from developing in this disease.

3] *Nutritional deficiencies.* In this age group, poor food habits, impoverishment with starvation, and poor vitamin absorption due to gastrointestinal disturbances such as gastric carcinoma, pancreatitis, malfunctioning gastroenteritic stoma, chronic diarrhea, and prolonged vomiting frequently result in a peripheral neuritis. The diagnosis, treatment, and prognosis were discussed in the previous section.

4] *Carcinomatosis associated with peripheral neuritis.* In this age group, one often is presented with a peripheral neuritis of gradual insidious course. When associated with loss of weight, developing anemia, or symptoms of a primary neoplasm, one should be aware of the relationship of these two entities. The most common neoplasm that is associated with a peripheral neuritis is the lung carcinoma. The peripheral neuritis may precede or be a late manifestation of the primary disease.

Treatment of this disorder consisting of general measures with restriction of motor activity and high-vitamin supplements of oral and parenteral route will frequently produce inprovement of neuritis, even in the presence of the progressing neoplastic lesion.

BREAST CANCER REMISSION is produced more frequently with diethylstilbestrol than with testosterone propionate. Combined therapy does not improve the remission rate of diethylstilbesterol alone. Objective signs of regression occurred in 3 of 22 patients given 100 mg. of intramuscular testosterone propionate 3 times a week, in 10 of 22 given 15 mg. of oral diethylstilbesterol daily, and in 9 of 22 given both drugs. Mean duration of improvement ranged from eight to ten months in all 3 groups.

B. J. KENNEDY, M.D., and JOHN H. BROWN, M.D., University of Minnesota, Minneapolis. Combined estrogenic and androgenic hormone therapy in advanced breast cancer. Cancer (Philad.) 18:431-435, 1965.

Functionally Corrected Transposition of the Great Vessels

Report of a Case Without Other Cardiac Malformation

M. M. DESHMUKH, M.B., M.R.C.P. (E), M.C.C.P.,
S. M. DESHMUKH, M.B., D.M.R.E., M. D. KELKAR, M.B., B.S.,
and P. K. SEN, M.S., F.A.C.S., F.C.C.P.

Bombay, India

UNTIL RECENTLY CONGENITAL corrected transposition of the great vessels of the heart was regarded as an extreme rarity. Schiebler and associates[1] reviewed the literature in 1961 and estimated the number of patients reported as 100. Of late, the condition is recognized more frequently because of the intensive investigation of patients with congenital heart disease. The incidence of corrected transposition in some of the catheterized series is approximately 3%.[2]

The definition of corrected transposition of the great vessels consists of 3 components:[2] (1) transposition, i.e., reversal of the anteroposterior relationship of the aorta and pulmonary artery with the result that the aorta lies anteriorly and the pulmonary artery posteriorly, (2) inversion, which is a change in the left-to-right relationship of the great vessels so that the aorta lies to the left and the pulmonary artery to the right, and (3) functional correction which permits oxygenated blood to pass to the aorta and the venous blood to the pulmonary artery. The course of circulation in this condition is as follows: The venous blood from the right atrium passes through a bicuspid valve to the right-sided ventricle which has the morphological characteristics of the left ventricle, namely, a smooth surface and 2 sets of papillary muscles. The pulmonary trunk arises from this ventricle and lies posterior and to the right of the aorta. Oxygenated blood from the left atrium passes through a tricuspid valve into the left-sided ventricle which has the morphological characteristics of the right ventricle, namely a trabeculated surface and the presence of crista supraventricularis. The aorta originates from this ventricle and lies anterior and to the left of the pulmonary artery. These 2 vessels run parallel to each other, and unlike in the normal heart, do not cross.

A variation in the situation described above may occur when the heart is in the right hemithorax, in situs inversus position, in which case the aorta lies anterior and to the right of the pulmonary artery. This is a rare variant and occurs in less than 10% of the cases of corrected transposition.[1] Rarely, this abnormality may occur in isolated dextrocardia. Merely a large shadow of the heart on the right side of the spine is not enough for a definite diagnosis of dextrocardia and situs inversus. As a result of inversion of the ventricles, the 2 chambers lie side by side in relationship to each other, rather than in an anteroposterior position. This may cast a larger shadow in the right hemithorax. Many of these cases are wrongly diagnosed as isolated dextrocardia. In true dextrocardia there is sinuatrial inversion which produces negative P waves in lead 1 of the electrocardiogram.

Corrected transposition of the great vessels, as a rule, is associated with other malformation of the heart, most often ventricular septal defect, pulmonary stenosis, and malformation of the atrioventricular valve on the left side. Isolated corrected transposition of the great vessels without other cardiac malformation is extremely rare and only 12 cases are reported in the literature (see table). In spite of the anatomical abnormality, the course of circulation is essentially normal in this condition. For this reason such cases may go unrecognized in life. In this communication we present the case report of a patient with functionally corrected transposition in whom in-

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M. M. DESHMUKH, S. M. DESHMUKH, M. D. KELKAR, *and* P. K. SEN *are with the Department of Surgery and Thoracic Clinic, K.E.M. Hospital and Seth G. S. Medical College, Bombay.*

TABLE

	Author	*Age (year)*	*Sex*	*Diagnosis*	*Clinical data*
1.	Graanboom[10]	33	M	Autopsy	Death due to renal failure
2.	Walmsley[11]	35	M	Autopsy	Heart block
3.	Edwards[12]	60	M	Autopsy	Died of peritonitis
4.	Platzer[3]	Adult		Autopsy	
5.	Platzer[3]	26	F	Autopsy	Tuberculous meningitis
6.	Schaefer[13]	36	M	Autopsy	Congestive cardiac failure due to sudden onset of heart block at age 25
7.	Goodman and Kuzman[14]	11	M	Angiocardiography	Clinically well
8.	Copestake[14]	42	M	Autopsy	Dextrocardia. Death due to right heart failure
9.	Copestake[15]	7	M	Angiocardiography	Dextrocardia. Asymptomatic
10.	Taussig[6]			Angiocardiography	Not given
11.	Cumming[5]	8	F	Angiocardiography	Heart murmur and fatigue
12.	Cumming[5]	3½	F	Angiocardiography	Heart murmur

vestigations failed to reveal any other associated major cardiac malformation. This patient developed symptoms after a murmur in the heart was detected and X-ray of the chest was interpreted as abnormal.

CASE REPORT

A 35-year-old male was referred to the Thoracic Surgery Department of the K.E.M. Hospital, Bombay, for cardiovascular evaluation. He complained of pain in the precordium and palpitation of six months' duration. The pain was sharp, related to exertion, one to two hours in duration, and occasionally radiated to the left arm. Relief of pain after cessation of exercise was variable. No relief was obtained with nitroglycerine. Examination showed a pulse rate of 100 per minute, with regular rhythm. The blood pressure was 120/75 mm. Hg. Maximum cardiac impulse was in the left fifth interspace medial to the midclavicular line. There was an ejection systolic murmur in the second left interspace. Pulmonary second sound was of normal intensity and normal split. The electrocardiogram (Fig. 1) showed a sinus rhythm with a rate of 90 per minute. Q.R.S. axis in the frontal plane was –30°, and the position of the heart was horizontal. T waves were inverted in leads AVL, V_5, and V_6. The Master's tolerance test was negative. X-ray of the chest was abnormal (Fig. 2). The cardiac-thoracic ratio was within normal limits. There was convexity along the left upper border of the heart, and the aortic knuckle and cardiac apex could not be defined. Descending aorta was seen along the left paravertebral border through the cardiac silhouette. The left atrium was not enlarged. The fundic air bubble was on the left side. The left dome of diaphragm was at the same level as the right. The lung fields and pulmonary vasculature were normal.

Right heart catheterization showed a right ventricular pressure of 40/2. The pulmonary artery was not entered. There was no evidence of left-to-right shunt at the atrial and ventricular level, and the peripheral oxygen saturation was normal.

Intravenous angiocardiogram showed the pulmonary artery and the right ventricular outflow shifted medially. The ascending aorta was shifted far to the left, corresponding to the convex configuration along the left upper half of the cardiac border noted in the plain X-ray of the chest. The ventricle draining into the pulmonary artery was smooth, to the right of midline, and the outflows of the 2 ventricles lay side by side. The pulmonary artery trunk appeared dilated (Figs. 3 and 4).

DISCUSSION

Corrected transposition of the great vessels without other major cardiac malformation is extremely rare. Only 12 patients are reported in literature and the table summarizes their salient features. Since the course of circulation in this condition is normal, Platzer,[3] who described 2 such patients, coined the term "functionally corrected transposition." This definition has been extended by Malers[4] to include cases of corrected transposition with abnormality of the left atrioventricular valve and other malformations without shunt such as pulmonary stenosis and coarctation of the aorta. However, in this communication, we are restricting to the cases without any significant cardiac malformation. In the patient reported by us, corrected transposition of the great vessels was the only abnormality. There

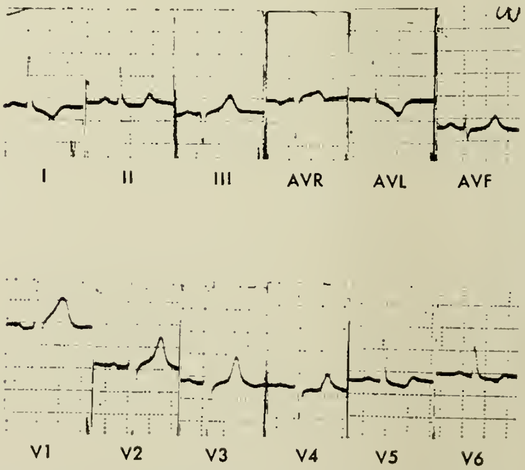

Fig. 1. Electrocardiogram shows left axis deviation and inversion of T waves in leads V_5 and V_6. Master's 2-step test was normal.

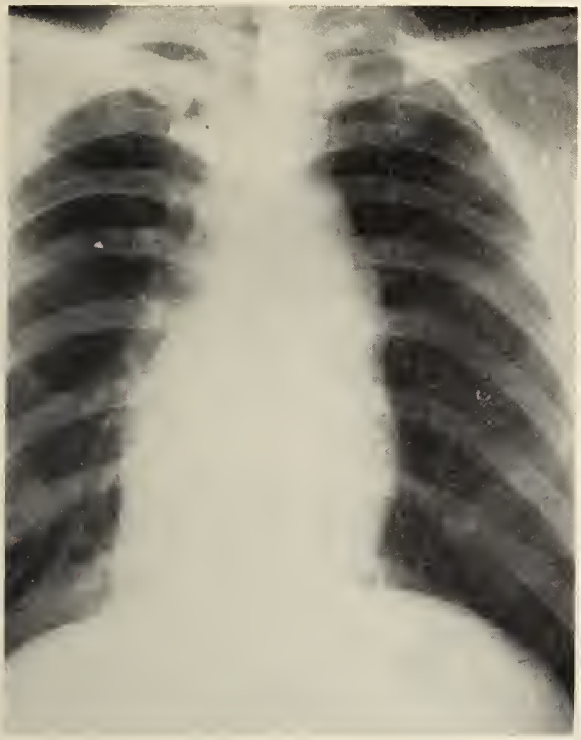

Fig. 2. Teleroentgenogram shows convexity along left upper border of heart. The cardiac apex and aortic knuckle are not clearly defined.

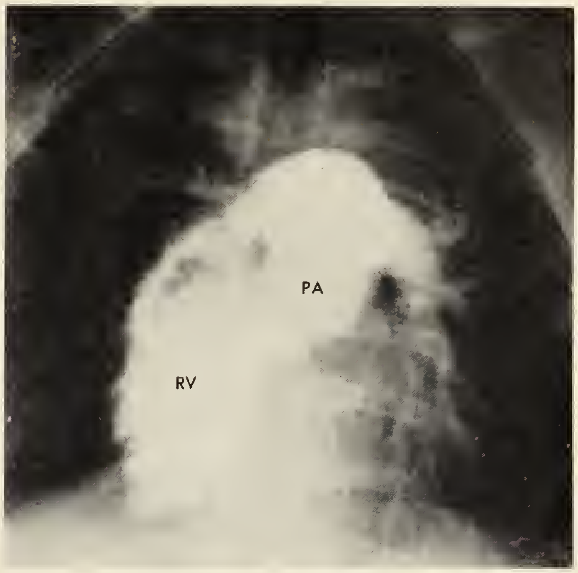

Fig. 3. The right ventricular outflow and pulmonary artery are shifted to right and ventricular outline appears smooth. The pulmonary artery is dilated. R.V., right ventricle; M.P.A., main pulmonary artery

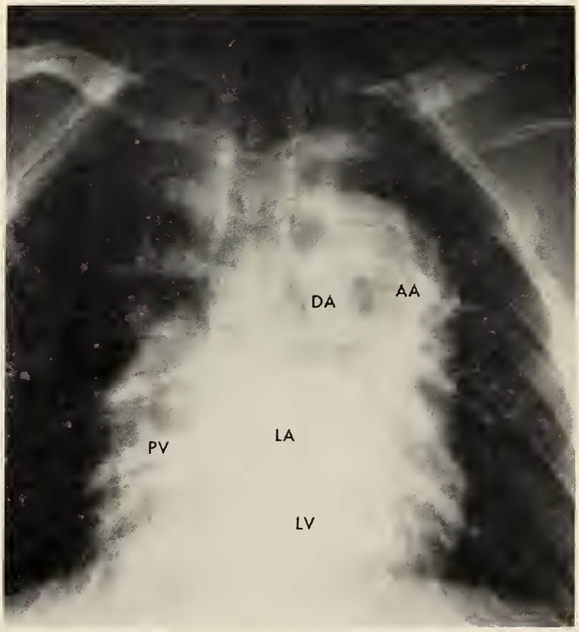

Fig. 4. Aorta lies to left of pulmonary artery and corresponds to convex configuration along left upper border of heart as seen in teleroentgenogram of chest. P.V., pulmonary vein; L.A., left atrium; L.V., left ventricle; A.A., ascending aorta; D.A., descending aorta

was no clinical, radiological, or hemodynamic evidence of other cardiac malformation.

Clinical picture in corrected transposition is usually dominated by the associated cardiac malformation and there are no typical clinical features characteristic of the isolated variety. Since the course of circulation is essentially normal, many of these patients may not have any symptoms. Our patient developed symptoms only after he was told of the murmur in the heart and abnormality of the roentgenogram which was interpreted as dextrocardia. On follow-up studies, the patient was relieved of his symptom after reassurance and explanation. Ejection systolic murmur in the left second interspace, which was present in our patient, was also noted by Cumming in 2 patients with functionally corrected transposition.[5] Intracardiac phonocardiography localized the site of production of this murmur in the outflow of the right ventricle. In his opinion, the murmur was generated by the sharp angulation of the ventricular outflow tract posteriorly to join the pulmonary artery. Similar distortion of the right ventricular outflow and the pulmonary artery was observed in our patient also. Gasul[6] observed that the second heart sound in the left second interspace was single but split over the second right interspace in cases of corrected transposition. However, this observation was not confirmed by several authors[1,7] who found the reduplication of the second heart sound in the second left parasternal interspace.

Electrocardiogram may provide diagnostic clues in patients with corrected transposition. Presence of QR pattern over the right ventricle and absence of this pattern over the left ventricle were noted in a significant percentage of patients by Anderson,[8] but this pattern does not appear in the absence of an associated defect. Left axis deviation and upright T wave in lead V_1 were observed in many of their patients by Schiebler[1] and Taussig.[9] Left axis deviation was also observed in our patient. Inversion of T waves in the left chest leads in our patient does not seem to be related to myocardial ischemia as the Master's 2-step test was negative. Heart block is frequently present in these patients and may develop suddenly, impairing the cardiac function.[1]

The X-ray findings, though considered not distinctive in corrected transposition with normal circulation, gave us the lead in the diagnosis. The convexity along the left upper border of the heart, which was interpreted as the ascending aorta, and poor definition of the aortic knuckle, in addition to a large portion of the heart on the right side of the spine, were considered characteristic of the corrected transposition. Cardiac catheterization and angiocardiography are the specific methods for a definite diagnosis of corrected transposition. The position of the "tricuspid" valve is shifted medially and the right ventricular outflow and pulmonary artery are shifted to the right in the frontal projection. This anomalous course of the catheter is quite diagnostic. It is often difficult to negotiate the catheter in the pulmonary artery. Simultaneously placed catheters in the pulmonary artery and the root of the aorta will clearly define the relationship of the great vessels in the frontal and lateral projections. The position of the great vessels and other chambers of the heart is best visualized by angiocardiography.

It seems reasonable to expect normal life expectancy in patients having corrected transposition of the great vessels without other cardiac malformation as the course of circulation is essentially normal. Advanced age has been reached by some of these patients and death has been due to noncardiac causes.[9,10] However, the prognosis in the reported cases had been variable. Heart block is a constant hazard in these patients. It usually develops suddenly after the age of 20, impairing cardiac function and leading to progressive cardiac failure.

SUMMARY

Corrected transposition of the great vessels is a complex malformation commonly associated with other cardiac defects. Isolated corrected transposition is extremely rare. These patients may escape detection or may be labeled as having serious cardiac malformation. Clinical picture, electrocardiogram, and X-ray of the chest, although atypical, may give valuable diagnostic clues. The final diagnosis is confirmed by means of a cardiac catheter and angiocardiography.

In spite of the anatomical abnormality, the course of circulation in this condition is essentially normal. The prognosis in the reported cases of the isolated variety of corrected transposition is variable. Advanced age may be reached, or the patient may develop heart block and die of progressive cardiac failure.

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Fates of Elderly Patients in an Intensive Therapy Program of a State Mental Hospital

RAMONA L. TODD, Ph.D., M.D.
Imola, California

During the first part of 1959, it was decided to intensify treatment efforts for elderly patients at Napa State Hospital, in the north bay region of California. The need for such attention had been brought into focus by the large number of elderly patients in various state mental hospitals, including our own, and the feeling by some that many of these patients might be released if therapeutic effort could be increased. The first step in the long-range program was to start a regimen for newly admitted women patients 65 years old and older. Later, a similar plan for men was added. The development of the main features of the program and its inception were concurrent as the chief basis for procedures and approaches was "trial and error." After five years of intensified therapy, a summing-up seems indicated.

A section of a smaller ward building, rather remote from the center of hospital activities, was made available as a receiving unit. The building was old and the interior was outmoded and inadequate. There were 39 beds, too many for the allotted space; however, it was considered that the site of the building was a greater handicap than its condition. The building has since been remodeled and now has 26 beds and adequate facilities. The staff was selected for their interest in old people as well as for training and professional qualifications. Included were psychiatric technicians, a social worker assigned part-time to the unit, and a physician who also had other duties. After five years of operation, this is still the general pattern except some recreational, occupational therapy, and other activities have been available from time to time. Physical therapy has also been provided. Consultation with medical specialties staff and all of the facilities of the hospital have been utilized.

The first patients were received March 9, 1959. Women on first admissions who did not require immediate care on medicine, surgery, the chest center, or the alcoholic program were sent to the unit.

From the beginning emphasis was placed on social service and on maintaining active relationships with relatives and close friends, with the ultimate goal of returning improved patients to their own communities. Thorough physical examinations and treatment were carried out promptly. Mental examinations, testing, and diagnoses were also done as soon as possible. The patients were immediately started on remotivation activities, and efforts were made to build a one-to-one relationship with a staff member, usually the psychiatric technician, who is the nursing group leader. Tranquilizers and electroconvulsive therapy were prescribed where appropriate. When the patient had become adapted to the milieu, an attempt was made to pair her with another patient who had been carefully selected. The idea being the development of an interdependent relationship so the ego strengths of each would be enhanced. When this was accomplished, the patient would begin to use group sessions for remotivation, resocialization, and where applicable, psychotherapy.

When the deterioration of the patient is still in the reversible stages, changes take place quickly and the patient is often ready to return to her community within four to six weeks or

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RAMONA L. TODD *is Senior Physician, Supervisory Charge of Geriatrics, Napa State Hospital, Imola.*

shortly after. If she had not improved by this time, she was transferred out of the program to one of the continued treatment units.

During the first six months of the program it became evident that it was worthwhile, and on Nov. 2, 1959, a similar program was started for men. The other half of the same building was used, and it also was remodeled and reduced to 26 beds.

Since the beginnings in 1959, the program has been operated along essentially the same lines, with the only significant changes being in our psychotherapeutic approach as the staff became more skilled in the treatment of elderly persons. This subject has been discussed in greater detail elsewhere.[1] There have been many personnel changes due to staff turnover or, occasionally, because someone did not relate well to older people or became depressed when faced with the problems of the aged. The staff has never been large nor has the program been supplied with equipment or services not generally available in the state mental hospital.

It is certain that figures do not project the picture of the dynamics of such a program as this; nevertheless, they indicate wherein lie the successes and failures and where the emphasis should be placed for further improvement in the future. It is in this spirit that the following story is told.

From the beginning through June 30, 1964, a total of 2,140 patients have been admitted to the program. In addition to these patients, the unit staffs also have received all patients 65 years old and older who are returned to the hospital from leave status, some who are under 65, and at times, the overflow from other units. All of these are excluded from this study which includes only the 2,140 newly admitted, over age 65 patients.

There were 1,196 women (Table 1) and 944 men in the total group. A study of the age groupings shown in the first 2 tables shows surprisingly little percentage difference of incidence between men and women in the 3 older age classes. If the ages are grouped into 2 categories, 65 to 79, and 80 and above, it will be seen that there is a difference of 4%, in that 31% of the women and 27% of the men are past 80. There are a few more women admitted than men even when the difference in length of time of the existence of the programs is considered, just as there are more women than men past 65 in the general population.

An average of about 4 women and 4 men per week have been admitted to the program since the beginning. This has meant, in terms of space alone, that the same number of patients must be released from the hospital or transferred to other units in the hospital.

TABLE 1

PATIENTS, 65 AND OLDER, ADMITTED TO GERIATRIC INTENSIVE TREATMENT PROGRAM, MARCH 7, 1959, THROUGH JUNE 30, 1964

Age at admission

	Men		*Women*		*Total*	
Age group	*No.*	*Percent*	*No.*	*Percent*	*No.*	*Percent*
65 to 69	212	22	278	23	490	23
70 to 74	241	26	262	22	503	24
75 to 79	232	25	293	24	525	24
80 to 84	181	19	230	20	411	19
85 to 89	57	6	105	9	162	8
90+	21	2	28	2	49	2
Total	944	100	1,196	100	2,140	100

TABLE 2

PATIENTS RELEASED FROM HOSPITAL

	Men		*Women*		*Total*	
Time after admission	*No.*	*Percent of men admitted*	*No.*	*Percent of women admitted*	*No.*	*Percent of all admissions*
Within one year	274	29	485	41	759	36
1 to 2 years*	27	4	23	2	50	3
2 to 5 years*	17	2	27	2	44	2
Total	318	35	535	45	853	41

*Calculated by number of patients admitted to program who have been in hospital indicated length of time. Only a small number of patients have been in five years.

Dealing with over 2,000 persons with a variety of mental illnesses ranging from purely functional to organic brain deficits, the staff has encountered many types of problems during the five years the program has been in progress. Varying degrees of success have resulted. For example, many more women have shown sufficient improvement to leave the hospital. Throughout the years of the present study, 41% of the women admitted have been released within one year after admission (Table 2) while only 29% of the men were released within one year. The number released after a year's hospitalization is small in either group. During the second year, 3% were released but this represents a total of 50 people. After two years and up until five years after admission, only about 1% of those originally admitted are released; however, 44 people in this group were able to leave the hospital by June 30, 1964.

It can be predicted now, with a fair degree of accuracy, that with therapeutic effort equal to

TABLE 3

DEATHS OF PATIENTS IN GROUP

	Men		*Women*		*Total*	
Time after admission	*No.*	*Percent of men admitted*	*No.*	*Percent of women admitted*	*No.*	*Percent of all admissions*
Within one year	282	30	318	27	600	28.0
1 to 2 years	34	4	61	5	95	4.4
After 2 years*	28	2	49	4	77	3.6
Total	344	36	428	36	772	36.0

*Patients in hospital varying lengths of time to June 30, 1964

that which was made during this program, 4 of every 10 persons admitted will be released from the hospital.

An interesting and encouraging finding is the low return rate among these elderly patients. Of the men, only 20 returned to the hospital within a year of release and only 1 after a year. This is an overall return rate of 6.6% for the men. The women had a higher rate but still lower than has been noted for all age groups in state hospitals. Within a year, 105 returned and later, 23 others came back. The 128 represent 24% of those who left. It is not known why these older men were better able to remain out than the women were. This topic suggests a separate study in itself.

A high incidence of deaths is usually a finding in any group of aged persons and this program has not been without this circumstance. During the first year after admission, a large number of patients expire from pneumonia, cardiovascular ailments, and other diseases of the elderly (Table 3). It will be noted that a few more men than women die during the first year of hospitalization, the difference being 3%. By the end of five years, 36% of both groups have expired.

What do these statistics mean in terms of planning for beds and space needed, personnel, drugs, equipment, and all the essentials of operating an ongoing, moving, changing program? Let us look at the first 80 patients, all of the women admitted between March 7 and June 30, 1959. After five years, only 8 are still in the hospital, 2 have been transferred to other hospitals, 33 are out of the hospital, and 37 are dead.

With an average group of 100 patients 65 years old and older admitted to such a program, it will be found that, at the end of a year, 36 will have improved and left the hospital, 5 will have relapsed and returned to the hospital, 28 will be dead, and 2 will have been transferred to other hospitals. Thus, 39 of the original 100 beds will be occupied.

Considering that many old people who find their way into state hospitals through court commitment are chronically sick physically, malnourished at the time of commitment, senile, and often alone, the release figure is perhaps the most remarkable of all the data. Observations during the first two years revealed that the release figure was too conservative to reflect the reversibility of mental disturbance in the aged. Another 6% improved sufficiently within a few months to leave the hospital but no place could be found for them to go. With the development of community resources, it can be expected that the next five years will result in fewer admissions and a greater number of releases so that more aged persons can live out their lives in familiar surroundings.

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M. B. Visscher, M.D.

WALLACE D. ARMSTRONG, M.D.
Minneapolis

Qualities of perserverance and industry derived from his Holland-Dutch ancestry and upbringing have been combined by Maurice B. Visscher with his creative imagination and acumen in work which has produced outstanding contributions in biomedical research, in medical education and administration, and in discussions of public affairs. He has earned well-deserved recognition in these fields or, in the case of the last named sphere, a reputation whose nature varies according to person, time, and circumstance. His most signal honors, derived from his research contributions and scientific statesmanship, are membership in the National Academy of Sciences and fellowship in the American Academy of Arts and Sciences. He has been almost continually and concurrently active in each of the fields named and, frequently, he seems to be at his best under conditions which would be those of intolerable turmoil for most men.

Dr. Visscher was born Aug. 25, 1901, at Holland, Michigan, the locale of Hope College, an institution founded in 1851 in the traditions and faith of the Dutch immigrants who settled and developed that part of the shore of Lake Michigan. Young Visscher received his A.B. degree in 1921 at Hope, where his work and interests in biology caused Prof. Frank N. Patterson to recommend him to the late Dean E. P. Lyon as a graduate student in physiology at the University of Minnesota. His advisor and mentor was Dr. Frederick H. Scott. His thesis for the Ph.D. degree, on the transport and storage of carbohydrate, was accepted in 1925. In 1931 Dr. Visscher completed the work for the M.D. degree at the University of Minnesota and during these medical studies he came under the special tutelage of Dr. George E. Fahr. It is fair to say that Visscher's research career was initiated, if not largely determined during his early years, by the influence and roles of Drs. Lyon, Scott, and Fahr. These men recognized the abilities of the young scientist, stimulated his interests, and provided him all facilities for research that the medical school then possessed. From 1925 to 1927 Dr. Visscher was a National Research Council Fellow while he studied and worked with E. H. Starling at University College, London, and A. J. Carlson at the University of Chicago during the period when these men were the giants of physiological research.

Dr. Visscher is unique among American physiologists in that his academic appointments since he received his Ph.D. have all been at the level of department head. He held the positions of associate professor and professor at the University of Tennessee from 1927 to 1929, and from 1929 to 1931 was professor and head of physiology and pharmacology at the University of Southern California. He returned to the Midwest in 1931 as professor and head of the department of physiology at the University of Illinois. In 1936 he was invited back to the University of Min-

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WALLACE D. ARMSTRONG *is professor and head, Department of Biochemistry, University of Minnesota, Minneapolis.*

nesota to head our department of physiology. In 1960 Dr. Visscher received the special award, Distinguished Service Professor of Physiology.

Dr. Visscher's scientific and scholarly writings are contained in 281 papers with 150 different persons as collaborators. It is obviously impossible to abstract even a fraction of these papers but an epitomy of his work in 3 fields of physiological science will show something of the magnitude and diversity of his contributions.

Cardiovascular physiology is probably the field in which Visscher is best known and it is certainly that in which he first attained distinction and repute. E. H. Starling had already established as his Law of the Heart the circumstance that the heart increases its work output by increase of its diastolic volume, which volume actually defines the myocardial fiber length at the beginning of systole. Visscher and Starling reported in a 1927 paper that oxygen consumption, which is a measure of the total energy produced by the heart, is also directly related to the diastolic volume. This paper, and subsequent contributions by Visscher and his collaborators, have made it clear that as the failing heart dilates in order to accomplish a given cardiac output and consequently increases its oxygen utilization, it does so with a decrease in the fraction of the total chemical energy converted to mechanical work. Thus, the failing heart is inefficient and a spendthrift of energy. The utility of the cardiac glucosides as drugs in heart failure was shown by Visscher and Peters to be due to their effect in restoring the metabolic processes in the myocardium toward normal. The heart is then enabled to do larger amounts of work at a given energy liberation and this spares its oxygen and fuel requirements. Stemming from these investigations with the isolated heart, and from a study in 1924 with Dr. F. H. Scott, is Dr. Visscher's continuing activity in the field of circulatory dynamics. He has had a special interest in factors affecting and regulating blood pressure in individual organs and body regions such as the pulmonary vascular bed. In recent years he has investigated the organ sites of disturbed vascular functions caused by the endotoxin of gram-negative organisms, which together produce the marked hypotensive condition of shock. A work of particular interest has shown that although the chemical mechanisms by which endotoxin affects cells is undoubtedly qualitatively alike in all animals there are, nevertheless, considerable quantitative differences between species in the responses of the various vascular beds to the endotoxin.

Water and ion absorption from the intestine and other luminal organs has been extensively investigated by Visscher and his collaborators. Visscher early recognized the value of isotopic tracers in this research and some of his most revealing results have been obtained through use of deuterium and radioactive sodium and chloride. The results have shown that there is a 2-way movement of water and of sodium and chloride ions between the intestinal contents and plasma during water and salt absorption. The rates of movement of water and salt out of the intestine are dissociated so that the fluid in the intestine becomes hypotonic with respect to the plasma as absorption progresses. An important deduction made by Visscher from these studies is that diffusion and osmosis are not adequate to account for intestinal absorption of even ions and water. Consequently, the intestinal epithelium performs osmotic work requiring the production and expenditure of metabolic energy in water and electrolyte absorption.

Cancer biology and some related nutritional factors in the mouse are subjects in which Dr. Visscher has been interested since the middle 1940s. In the dietary studies particularly, he has had the effective collaboration of his friend of many years and fellow physiologist, Dr. Joseph T. King. These studies have shown that caloric restriction delays the onset of spontaneous mammary carcinoma in mice and acts to prolong the period of fertility and increase the longevity of nontumor-bearing female animals. The latter effect is still evident even when the animals are fed normally after a prolonged period of restriction. In another connection it was found that a semipurified diet, when fed to male mice, resulted in the development of a species with "heart failure." The incidence of this cardiac abnormality could be reduced, or its age of onset prolonged, by either caloric restriction alone or by an increase of vitamin E.

Related both to Dr. Visscher's research activity and to his role as a teacher of graduate students is his record of accomplishment as advisor to 29 students who have earned the Ph.D. degree at the University of Minnesota.

Dr. Visscher has had, through his abilities and special attention to administrative and advisory duties, a marked effect on the extent and direction of progress of the medical school over the last three decades. Under his direction the department of physiology has had an immense growth in quantity and quality of staff and in space and facilities, with the result that this department is now the preeminent department of physiology in research and graduate research training in this country. All of this has required imagination and insight to conceive new projects or enlargement of others, and a more than common ability to obtain financial support. Dr. Harold S. Diehl and Dr. Robert B. Howard, as deans of the College of Medical Sciences, have been as responsive to Dr. Visscher's requests as resources permitted. They have done so because they have had confidence in the value and productivity of Dr. Visscher's enterprises and have known that university support facilitates the acquisition of outside funds. Among the agencies which have aided Dr. Visscher's research, or the growth and work of his department, are the United States Public Health Service, the Hill, Macy, and Rockefeller Foundations, the American Cancer Society, the American Heart Association, the Minnesota branches of the last 2 agencies, the Sievertsen Fund, and the Barber Oil Company of Minneapolis.

Dr. Visscher's foresight and effective planning, mainly carried out through special fund arrangements, have been responsible for obtaining the services of some of our best known and distinguished staff members. Among these are Drs. Ancel Keys, John J. Bittner, Herbert Freundlich, Karl Sollner, Victor Lorber, and Carlos Martinez.

It is probable that no major activity or innovation in the medical school during the last thirty years has escaped Dr. Visscher's attention and influence. He is a valued counselor on formal and ad hoc committees and his advice and suggestions are freely offered by him and are sought by his colleagues, associates, and university officials. Dr. Visscher is an energetic and compulsive man about his own plans, projects, and ideas. He rarely gives any evidence of self-doubt about his position in discussion of these or hesitancy in their promotion. The result is that he can be more than a little vexing at times. Nevertheless, it can be said that while Visscher is not always right he is seldom wrong.

Dr. Visscher has been a useful advocate on the state and national scenes in measures of importance to medical science and education. A few examples of this nature can be cited. He has been continually aware of the hazards to progress of that group of persons who seek to prevent the use of animals in scientific research and in the training of medical practitioners. He has been unrelenting in his opposition to their more restrictive proposals, and effectively so, since the time in Chicago in the early 1930s when he vanquished the actress Irene Castle McLaughlin in debate. At the present time, Dr. Visscher takes an active role in support of a realistic animal care bill before congress which would obviate the severe limitations on medical research contained in bills supported by the antivivisectionists. He has served as vice-president and president of the National Society for Medical Research, an organization which supplies information about the use of animals in biomedical research to legislative bodies and combats the exaggerated or uninformed assertions of the groups opposed to animal experimentation.

Dr. Visscher was a member of the Council of the American Association for the Advancement of Science from 1941 to 1946 and vice-president of the American Heart Association from 1950 to 1962. He now serves as chairman of the scientific advisory committee of the newly established American Medical Association Education and Research Foundation Basic Biomedical Research Institute. He promotes medical care and its distribution through his chairmanship of the medical control board of the Group Health Plan of Minnesota, and he helps to provide up-to-date and succinct medical information to practitioners by his service as editorial consultant to *Modern Medicine.*

Dr. Visscher has had a longtime interest and role in international scientific affairs. For example, he has served on the council and was president, from 1952 to 1953, of the International Organizations of Medical Sciences. He was secretary-general from 1953 to 1959 of the International Union of Physiological Sciences, the organization which is responsible for the triennial Physiological Congress. He was a member of a nutrition survey team under the auspices of the United Nations Relief and Rehabilitation Administration and the Unitarian Service Committee to Italy from 1945 to 1946. With the support of the World Health Organization he served as chairman of a medical education mission to Austria in 1948.

Dr. Visscher's work and interests in physiology as a research field and as an important subject in the medical curriculum has led him to take an active part in the work of the American Physiological Society and related affairs. He has served that society as secretary (1944 to 1948), president (1948 to 1949), and chairman of the board of publication trustees (1955 to 1959). Since 1953 he has been a member of the board of directors of Annual Reviews, an organization which publishes yearly reviews of selected subjects in medical science, physics, chemistry, and mathematics. An especially noteworthy activity in the field of literature compilation and synthesis is the *Handbook of Physiology* of which Dr. Visscher has been editorial board chairman since 1958.

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Book Reviews . . .

Complement

edited by G. E. W. WOLSTENHOLME *and* JULIE KNIGHT, *Ciba Foundation Symposium, 388 pp., ill., Little, Brown & Co., Boston, 1965. $12.50*

This is another monograph in the Ciba Foundation Symposium series and, like its predecessors, is a notable contribution to medical and chemical research.

The great importance of complement has been apparent ever since the recognition of its existence some seventy years ago, because its cytotoxic properties are striking and seem to explain, in part, the protective attributes of antibody. The inclusion of a chapter on this subject in the "Annual Review of Microbiology 1965" is an indication of current interest.

The papers in the Ciba Symposium help to throw more light on this "twilight zone," but we are still far from a complete elucidation of the reactions involved. One important aspect of this symposium is the clarification of the language of complement components. Although workers may employ different letters and numbers, they now know when they are discussing the same component, because clarifying identity tests are available. The book presents 15 papers, all by outstanding authorities, and, as in the other Ciba Symposia, each is followed by a complete account of the discussion. In many instances, the issues raised in the discussion are more exciting than the papers. In all cases, the complete and uninhibited give-and-take clears up obscure points and occasionally brings forth a compromise. For example, in his paper "Mechanisms of Haemolysis by Complement," Dr. Mayer, of Johns Hopkins, offers a criterion of complement involving the complete sequence of reactions. After the debate, he willingly modified his stand and agreed that immune adherence does not go all the way to lysis and that other phenomena such as leukocyte emigration or phagocytosis can be stimulated at levels short of cell lysis. The brilliant paper by Dr. Thorbecke and her associates gives us the only insight, up to now, of where complement arises and how fast it is turned over.

It now seems clear that several of the component parts of complement exist in the serum as precursors, activated by interaction with antigen and antibody complexes. Experimental evidence presented by Dr. Henry J. Winn indicates that the action of complement on sensitized nucleated cells is like that on sensitized mammalian erythrocytes, and future studies will emphasize "the rôle of complement . . . [in the sensitization of] various kinds of cells to the destructive effects of designated species of complement." In his paper, Dr. Louis H. Muschell suggests that, by analogy with mammalian cells without a cell wall, complement may damage the bacterial cell membrane, rending it susceptible to lysis or spheroplast formation. The paper on phagocytosis by Drs. S. U. Boyden, R. J. North, and S. M. Faulkner is particularly outstanding. Another important revelation is the use of cellulase for removing the receptors for conglutinin and B_{1C} protein. This opens up a field for the use of available tools to attack the problems at an empirical level.

Besides the expected tables, graphs, and line drawings, the book contains a number of excellent photographs of immunoelectrophoretic patterns and some striking electron micrographs showing plainly the holes in the surface of the membrane of a lysed cell. A complete author index is helpful, but the subject index is rather skimpy.

This book is highly technical and definitely for the specialist. To the outsider, work on complement becomes more and more complicated and obscure. The increasing use of mathematical symbols in an apparently artificial system will deter the uninitiated. However, the practicing immunologist and the investigator in this field will find this book important and enlightening.

DAVID B. SABINE
Yonkers, New York

Anatomy and Surgical Technique of Groin Dissection

by JOHN S. SPRATT, JR., M.D., WILLIAM SHIEBER, M.D., F.A.C.S., *and* BURL MAYES DILLARS, M.D., *97 pp., ill., C. V. Mosby Co., St. Louis, 1965. $9.75*

This monograph is a presentation of the compiled clinical data of ilioinguinal lymph node dissection en bloc on 148 cancer patients treated at Ellis Fischel State Cancer Hospital, Columbia, Missouri, since 1941. The material is on epidermoid cancers, melanomas, and adenocarcinomas and on sarcomas of the lower trunk and extremities, where the malignant disease metastasizes to the ilioinguinal lymph nodes. Their social service department made a complete follow-up on all the cases.

The authors have detailed the anatomy of the ilioinguinal area in a lucid manner. The illustrations are excellent and clarify adequately. Lymphangiography is used, and the authors show how valuable the procedure is in evaluating the problem of ilioinguinal lymph node metastases. The procedure is used preoperatively to obtain information regarding the need for surgery, and postoperatively to determine the adequacy of the operation.

Their technique of ilioinguinal lymph node dissection is meticulously described. The technique is planned and performed on a well-conceived anatomic concept. The dissection is performed in an orderly manner. The description of the dissection is well illustrated at the various stages of the operation. The illustrations are well detailed and supplement the description of the technique in a clear, understandable manner. The authors have been careful to perform a dissection for the complete ablation of the lymph node bearing tissue in the inguinal and iliac areas.

A section of the monograph is devoted to the indications they used for the ilioinguinal lymph node dissection. Their experience and results are well tabulated for the various malignant problems that were treated. This monograph contains valuable material for residents in surgical training and for surgeons who care for malignant diseases of the lower trunk and extremities.

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News Briefs . . .

North Dakota

DR. WILLIAM C. HURLY of Minot has been elected president of the Northwest District Medical Society. He succeeds Dr. Gale R. Richardson. Other new officers, both of Minot, are Dr. Lloyd A. Giltner, vice-president, and Dr. B. Jayapathy, secretary.

* * * *

DR. LLOYD S. RALSTON, internist, has opened a practice in Grand Forks. Dr. Ralston practiced at Larimore from 1948 to 1960 and at Bismarck from 1960 to the present.

* * * *

DRS. CHARLES A. HAMILTON and RICHARD W. FARDAL have been elected to the board of the Bismarck Medical Foundation, a subsidiary of the Quain and Ramstad Clinic, which finances research projects for the clinic staff and provides scholarships for nurses, medical, and paramedical students.

* * * *

DR. LEONARD KLASSEN has joined the staff of the Rollette and Dunseith Medical Clinics as an associate with Drs. Stuart J. Cook and John Sawchuk. Dr. Klassen and family have moved to Rollette from Milk River, Alta., Can.

* * * *

DR. PERRY H. ENGSTROM, JR. of Wahpeton has volunteered for Project Vietnam. Dr. Engstrom flew to Saigon Feb. 1 for a tour of at least two months.

DR. WILLIAM T. POWERS has been elected chief of staff of St. Michael's Hospital, Grand Forks, succeeding Dr. John J. McLeod. Other members of the board are Drs. Rodney G. Clark, vice-president; John H. Graham, secretary; James A. Leigh, William C. Nelson, and Keith G. Vandergon, committee members.

* * * *

DR. RAYMOND L. COULTRIP, JR. has left the Community Hospital in McVille for Vietnam as a member of the Special Armed Services.

* * * *

DR. JOHN M. BROOKS of Johnson City, Tenn., has joined the staff of the Public Health Service Indian Hospital at Fort Yates.

* * * *

DR. WILLIAM G. NULL has resigned from the Quain and Ramstad Clinic, Bismarck, in order to take up practice at Salina, Kans.

* * * *

DR. ROBERT F. NUESSLE has been reelected president of the medical staff of the Bismarck Hospital. All other officers were also reelected: Dr. Marlin Johnson, vice-president, and Dr. Robert B. Tudor, secretary. Members-at-large are Drs. Clifford H. Peters and Robert R. Kling.

* * * *

DR. W. L. POTTS has resigned as superintendent of the North Dakota State Tuberculosis Sanatorium, San Haven.

* * * *

DR. DUANE F. PANSEGRAU, a surgeon, has joined the Grand Forks Clinic staff. Dr. Pansegrau received his medical degree in 1956 from the University of Iowa and practiced at Marshfield, Wis., before coming to Grand Forks.

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DR. PETER MORRISON of Eastend, Sask., Can., has established practice at the Towner Clinic.

* * * *

DR. GERALD T. SAILER of the Hettinger Clinic has been elected to active membership in the American Academy of General Practice.

* * * *

DR. DOUGLAS PYE of the Community Clinic, Elgin, has been elected to active membership in the American Academy of General Practice.

* * * *

DR. ROBERT C. PAINTER of Grand Forks has been elected president of the Third District Medical Society. He succeeds Dr. Kenneth S. Helenbolt of Grand Forks. Other officers are Dr. Harold I. Tarpley, Jr., president-elect, and Dr. Thomas L. Schafer, secretary-treasurer, both of Grand Forks; and Dr. Curtis W. Sande, vice-president, of Northwood. Medical association delegates are Dr. George L. Countryman of Grafton and Drs. John A. Sandmeyer, Richard H. Leigh, Kenneth S. Helenbolt, Harold W. Evans, and William T. Powers, of Grand Forks.

* * * *

DR. WALTER C. HANEWALD has been elected chief of staff of St. Joseph's Hospital, Dickinson, succeeding Dr. Andrew C. Sawchuk. Dr. Donald J. Reichert is vice-president and Dr. Ralph J. Dukart is secretary.

Minnesota

DR. FRANKLIN C. ANDERSON has been elected president of the Owatonna City Hospital. Other new officers are Dr. James E. McEnaney, vice-president, and Dr. Robert T. Hilker, secretary. Outgoing president is Dr. Donald H. Dewey.

* * * *

DR. MERLE S. MARK of Minneapolis has been elected chief of the medical staff at Glenwood Hills Hospitals, Golden Valley. Serving with him will be Dr. John W. Lawrow, vice-chief of staff, and Dr. Walter Indeck, secretary-treasurer. Dr. Mark succeeds Dr. Harry W. Mixer.

* * * *

DR. WERNER E. KAESE has been elected president of the medical staff of Olmsted Community Hospital, Rochester. Other officers named for the coming year are Dr. Clayton J. Bennett, president-elect, and Dr. Thomas L. Peyla, secretary-treasurer. Dr. Harry F. Burich is the immediate past-president.

* * * *

DR. ELDORE B. NASH has been elected chief of staff of North Memorial Hospital, Robbinsdale. Other committee members include Drs. H. Robert Ransom, chief of staff elect; Frederick M. Hass, past chief of staff; and Gordon E. Johnson, secretary-treasurer.

* * * *

DR. C. WALTON LILLEHEI, professor of surgery at the University of Minnesota Medical School, has been elected president of the American College of Cardiology.

* * * *

DR. ORVILLE P. SWENSON of Cloquet has been inducted into the armed forces and is in training at Fort Sam Houston, Tex.

* * * *

DR. TRACY E. BARBER, Austin, has been named general chairman of the meat packing, tanning, and leather products section of the National Safety Council. Since 1949 Dr. Tracy has been medical director of George A. Hormel and Co., Austin.

(Continued on page 14A)

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NEWS BRIEFS

(Continued from page 13A)

DR. CHESTER L. SHEEDY, Austin general practitioner and obstetrician, has retired from private practice and accepted a position in the out-patient clinic at the Veterans Administration Hospital at Fort Snelling. Following a tour to Mexico, Dr. and Mrs. Sheedy will establish residence at Fort Snelling.

* * * *

DR. ROGER W. BROCKWAY of Grand Rapids has been elected president of the Range Medical Society. Other new officers are Drs. Henry W. Johnston, Virginia, president-elect; Kenneth E. Ahola, Hibbing, vice-president; and Douglas J. Coy, Grand Rapids, secretary-treasurer. Delegates are Drs. Richard E. Barnes, Aurora; Luverne W. Johnsrud, Hibbing; and Robert T. Kelly, Grand Rapids.

* * * *

EIGHT NEW PHYSICIANS HAVE BEEN APPROVED as members of the staff of the Northfield Hospital, and one osteopathic physician has been granted associate membership privileges. The eight are Drs. J. Gordon Beaton, Roy H. Good, Jack F. Haas, David C. Halvorson, John W. Hanson, Stanley T. Kucera, G. N. Rysgaard, and Bernard Street. Dr. Dale Dodson is the osteopathic physician.

* * * *

DR. FRANCIS W. CONLEY has been elected chief of staff at St. Luke's Hospital, Duluth, succeeding Dr. John J. Halbert. Dr. Karl E. Johnson is new president-elect. Department and section heads are Drs. Phillip V. Halliday, internal medicine; Roy R. Juntunen, infirmary; George M. Cowan, neuropsychiatry; John C. Feuling, orthopedics; Jack E. Wall, obstetrics; and Roy J. Thurn, general practice.

DR. LAWRENCE R. BOIES, JR. of Hopkins has begun practice in the Wayzata Medical Building. Dr. Boies is an otolaryngologist.

* * * *

DR. THOMAS M. RECHT has been elected chief of staff of the Eitel Hospital, Minneapolis. Other new officers are Dr. Richard E. Anonsen, assistant chief of staff, and Dr. Marie Moorhead, secretary-treasurer.

* * * *

DR. LESTER N. DALE has joined the staff of the Hastings Medical Clinic in association with Drs. Herman J. Just and John W. Foderick.

* * * *

DR. DANIEL K. HALVORSON has been reelected president of the Steele County Medical Society and delegate to the board of Minnesota Blue Shield. Other officers are Drs. John C. Henry, vice-president; D. L. Adams, secretary-treasurer; and Theodore W. Stransky, alternate delegate.

* * * *

DR. FREDERIC T. BECKER has been installed as chief of staff of St. Mary's Hospital, Duluth, succeeding Dr. Daniel R. Goldish. Other officers are Drs. Ivan T. Clark, chief of staff elect, and Howard J. Meyer, secretary. Chiefs of service are Drs. William H. Goodnow, medicine; S. Sverre Houkom, orthopedics; Peter J. Bartzen, obstetrics; Malcom M. Fifield, urology; William J. Slack, eyes, ears, nose, and throat; and Karl W. Emanuel, general practice.

* * * *

DR. JOHN H. ALLEN has been named chief of staff at the Chippewa County–Montevideo Hospital, succeeding Dr. Ludvig R. Lima. Other officers are Drs. Thomas G. Birkey, vice-chief of staff and secretary; Henry A. Roust, Jerome L. Kremer, and Norman L. Hagberg are executive committee members.

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NEWS BRIEFS

DR. VINCENT R. HUNT of Red Lake Falls has been named president of the Red River Valley Medical Society. Other officers are Dr. Clifford J. Stadem of Twin Valley, vice-president, and Dr. Russell O. Sather of Crookston, secretary-treasurer. Delegates, both of Thief River Falls, are Drs. George B. Martin, Jr., and Earl W. Dagg, alternate.

* * * *

DR. CHARLES W. FROATS has been elected chief of staff at St. Luke's Hospital, St. Paul. Other new officers are Drs. Irvine M. Karon, vice-chief of staff; Thomas W. Votel, executive committee member-at-large; and Joseph M. Barnett, secretary-treasurer. Dr. Robert E. Lindell was elected chief of medicine and Dr. C. Robert Baker, chief of general practice.

* * * *

DR. WILLIAM J. KANE, assistant professor of orthopedic surgery at the University of Minnesota, has been named a winner of a Kappa Delta award for contributions to orthopedic surgery. The award is presented by the American Academy of Orthopedic Surgeons.

* * * *

DR. JOHN B. LA LONDE has joined the medical staff of the Bemidji Clinic. Dr. LaLonde has just completed a four-year residency in surgery at the Philadelphia General Hospital.

* * * *

DR. DONALD L. CARLSON has been elected chief of staff at St. Ansgar Hospital, Moorhead. Other new board members are Drs. Richard H. Seifert, vice-president; Hagbart G. Rice, secretary-treasurer; and Dale C. Kana, member-at-large.

* * * *

DR. GORDON E. LEE of Glenwood has been elected to active membership in the American Academy of General Practice.

* * * *

DR. RICHARD J. FREY has been elected chief of staff of St. Barnabas Hospital, Minneapolis. He succeeds Dr. Archie M. Smith who will serve as councilor for the hospital. Dr. John E. Smith has been elected vice-chief of staff and Dr. Stanley H. Calin, secretary-treasurer.

* * * *

DR. CLAUDE R. HITCHCOCK, chief of surgery at Hennepin County General Hospital, has been appointed head of a cancer-detection program cosponsored by the Hennepin County Unit of the American Cancer Society and an unnamed donor. Using thermographic techniques, doctors at General Hospital will inspect the breasts of 4,000 Minneapolis women, all volunteers.

* * * *

THE MANKATO CLINIC has added three new physicians to its staff. They are Dr. Gail W. Haut, radiologist, Price, Utah; Dr. Joseph A. Heaney, psychiatrist, Philadelphia, Pa.; and Dr. Henry C. LaBrec, dermatologist, LaCrosse, Wis.

* * * *

DR. CARL D. EKLUND, has been elected chief of staff of Miller Memorial Hospital, Duluth. Dr. Francis W. Conley is the new vice-chief of staff, and Dr. John B. Sanford, secretary-treasurer. Dr. William J. Slack was elected as a new member of the executive committee.

* * * *

DR. GEORGE M. MIKS will begin practice in the Eveleth Clinic April 1. Dr. Miks received his medical degree from the University of Marquette in 1963 and is at present a staff member of the clinic at Ely.

(Continued on page 16A)

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(Continued from page 15A)

South Dakota

DR. JAMES S. FERGUSON of Middlesex, Vt., has established practice in Murdo. A native of Australia, he came to the United States in 1947 and became a citizen in 1951. Dr. Ferguson received his medical degree from the University of Buffalo (N.Y.) School of Medicine.

* * * *

DR. LOWELL P. SWISHER, Kadoka, has been elected to active membership in the American Academy of General Practice.

* * * *

DR. LEONARD W. TOBIN has been elected president of the medical staff of St. Joseph Hospital, Mitchell. Other officers are Dr. Richard D. Hockett and Dr. James L. Vose. Elected to the executive committee were Dr. William A. Delaney and Dr. Oscar J. Mabee.

Deaths . . .

DR. FRED L. BLAIR, JR., 59, chief of staff of the outpatient clinic, Veterans Administration, Fort Snelling, died Feb. 4. Dr. Blair received his medical degree from the University of Iowa in 1938.

* * * *

DR. HAROLD F. WAHLQUIST, 72, Minneapolis physician, died Feb. 9 at his home. Dr. Wahlquist received his medical degree from the University of Minnesota in 1925. He was a former chief of staff at Methodist Hospital and a charter member of the Minneapolis mayor's mental health board to organize a psychiatric clinic at Hennepin County General Hospital.

* * * *

DR. OLIVER E. SARFF, 65, Duluth physician and urologist, died Jan. 16 after a long illness. Dr. Sarff received his medical degree from the University of Minnesota in 1930 and began practice in Duluth in 1946. He was a member of the American College of Surgeons, the American Board of Urology, and the American Urological Association.

* * * *

DR. GEORGE U. IVERS, 59, Cass County North Dakota health officer and Fargo physician, died Jan. 26. Dr. Ivers received his medical degree from Rush Medical College, Chicago, in 1932. In addition to his other work he had been associated with the Veterans Administration and the Northern Pacific Railway.

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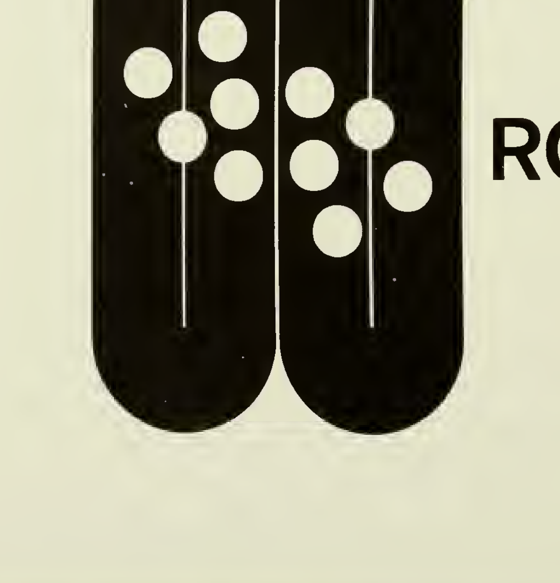

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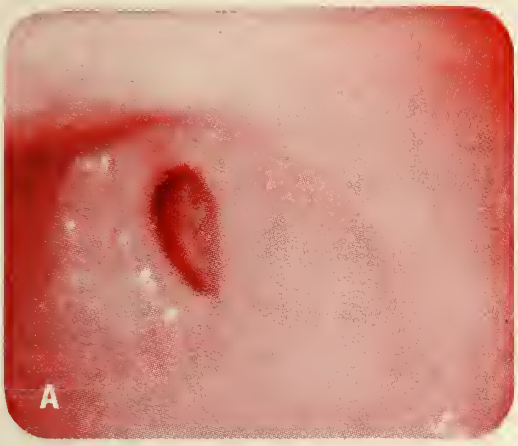
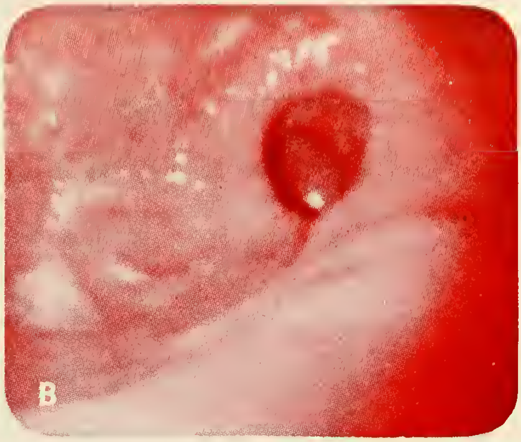


Which Is Pyloroplasty with Vagotomy?



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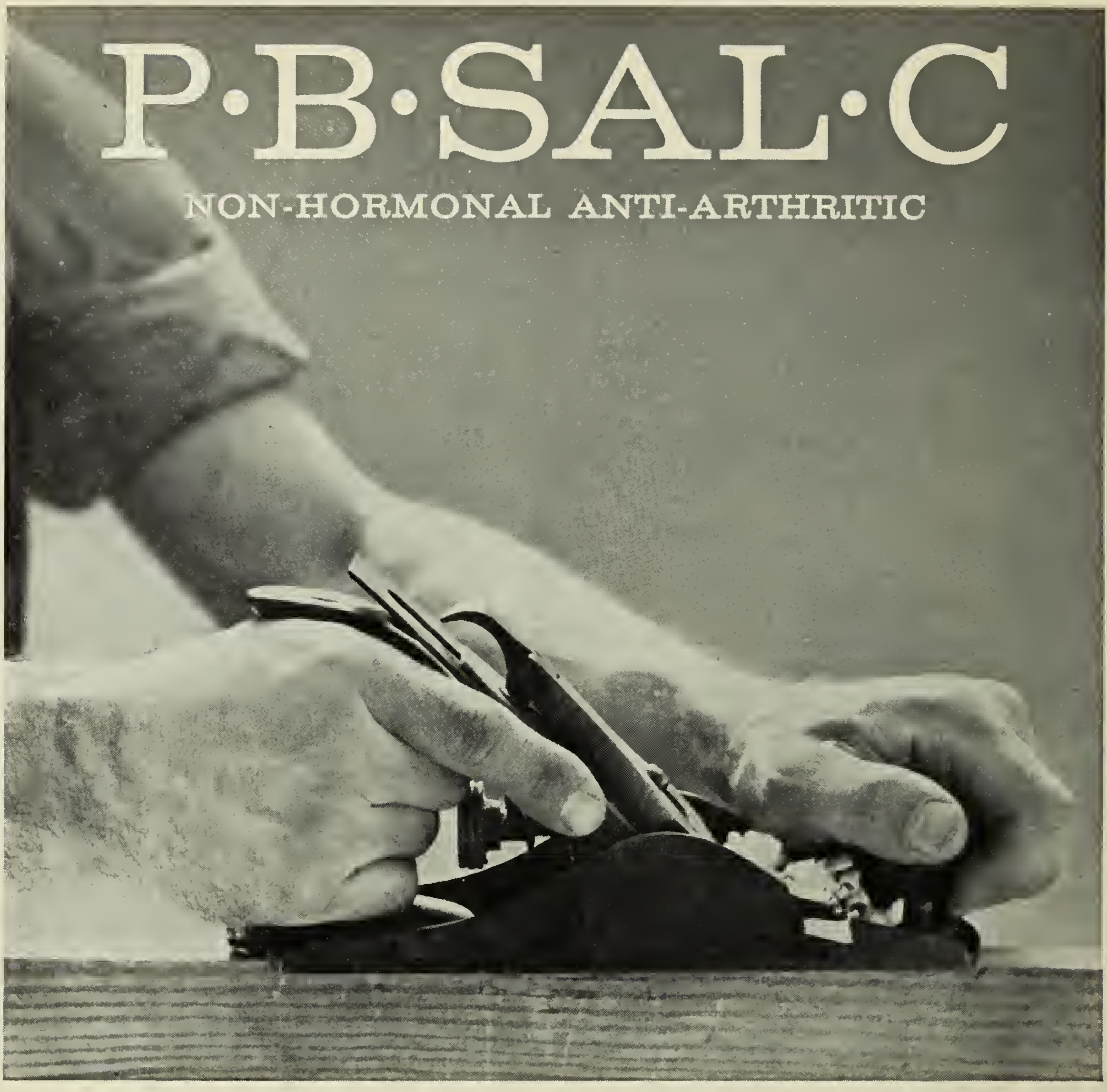

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With the increase of highway traffic accidents, more and more physicians are called upon to give emergency treatment to the patients with multiple injuries. If all significant derangements are to be recognized, a method for determining the full extent of injury and for establishing priorities for treatment is essential.

The June issue of THE JOURNAL-LANCET is addressed to this problem. The articles have been contributed by members of the staff of the St. Paul–Ramsey (Ancker) Hospital. Their recommendations are based on a large experience with management of traumatic injuries. Guest editor is John F. Perry, Jr., M.D., Chief of Surgery at St. Paul–Ramsey, who has contributed the "Introduction" and an article, "Management of Thoracic Injuries." Other articles are:

- **The Evaluation and Initial Treatment of the Accident Victim,** Robert A. Van Tyn, M.D.
- **The Emergency Care of Cerebral Injuries,** Wallace P. Ritchie, M.D.
- **Vertebral Column Injuries,** Max E. Zarling, M.D.
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- **Trauma to the Urinary Tract,** A. A. Hakim, M.D., and Nasser Javadpour, M.D.
- **Eye Injuries,** Robert Hugh Monahan, M.D., and Charlotte Weeks Hill, M.D.
- **Perforations of the Colon and Rectum,** William C. Bernstein, M.D.
- **The Emergency Treatment of Burns,** James W. LaFave, M.D.
- **Blunt and Penetrating Wounds of the Abdomen,** Harlan D. Root, M.D.
- **Extremity Fractures in the Patient with Multiple Injuries,** Frank S. Babb, M.D., Wayne W. Thompson, M.D., and Robert B. Winter, M.D.
- **Trauma to the Female Genitalia,** Erick Y. Hakanson, M.D.
- **The Facial and Laryngeal Injury,** Jerome A. Hilger, M.D., Douglas R. Kusske, M.D., Albert Hohmann, M.D., and Barclay M. Cram, M.D.

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The Evaluation and Management of the Patient with Hypertension

RONALD OLIN, M.D.

Fargo

One of the most common and important problems confronting the medical practitioner today is the evaluation and management of the patient with hypertension. It has been estimated that 5% of the adult population of the United States has hypertension, and it is related to the cause of death in 20 to 30%.

Most practitioners accept 150/90 as the upper limit of normal after age 15, although some accept up to 160/100. Hypertension, as defined by the conference on "Methodology in Epidemiological Studies of Cardiovascular Disease" (1960) sponsored by the American Heart Association, is a pressure of 160/95 or greater.[1] Incidence of hypertension increases with age and is more common in the female, who seems to tolerate it better. Thus, a diastolic pressure of 120 mm. Hg has an entirely different meaning in a man of age 35 than in a woman of age 65. Studies by the Metropolitan Life Insurance Company, based on its own findings and those of the Society of Actuaries (1959), show that any degree of sustained hypertension adversely affects longevity. For example, in a male aged 35, the normal life expectancy is forty-one and one-half years; if his blood pressure is 150/100, the expectancy is reduced to twenty-five years.

Hypertension follows a definite morbid course, eventually associated with vascular impairment of the brain, fundi, heart, kidneys, and peripheral vessels. When organ damage results, symptoms and signs of its insufficiency appear. Thus, the natural history reveals that some 40% of hypertensive patients die of congestive heart failure, 35% die of coronary artery disease, 15% die of cerebrovascular accidents, and 10% die of uremia.

The objectives of a careful evaluation of the hypertensive patient are to determine if the blood pressure is [1] labile or sustained, [2] primary or secondary in etiology, and [3] uncomplicated or complicated by vascular impairment.

The objectives of treatment are [1] to increase comfort by alleviating symptoms and [2] to prevent or reverse complications, thus prolonging life.

CLASSIFICATION OF HYPERTENSION

To evaluate a patient with hypertension, the following classification should be kept in mind:

- I. Systolic hypertension (over 150 mm. Hg) due to
  - A. Atherosclerosis
  - B. Aortic insufficiency
  - C. Thyrotoxicosis
  - D. Complete heart block
  - E. Patent ductus arteriosus
  - F. Arteriovenous aneurysm
  - G. Anemia
  - H. Paget's disease of bone
  - I. Psychogenic
- II. Systolic and/or diastolic hypertension (over 90 mm. Hg)
  - A. Primary (essential)
  - B. Secondary
    - 1. Renal
      - a] Acute glomerulonephritis
      - b] Chronic glomerulonephritis

RONALD OLIN *is with the Department of Internal Medicine, Fargo Clinic, Fargo.*

- c] Chronic pyelonephritis (unilateral or bilateral)
- d] Obstructive uropathy (unilateral or bilateral)
- e] Polycystic disease
- f] Diabetic glomerulosclerosis
- g] Collagen diseases
- h] Muliple renal infarcts (unilateral or bilateral)
- i] Radiation nephritis
- j] Tumors
- k] Renovascular (unilateral or bilateral)
  - [1] Intrinsic
    - [a] Atherosclerotic plaque
    - [b] Fibromuscular medial hyperplasia
    - [c] Embolism
    - [d] Renal artery aneurysm
    - [e] Syphilitic arteritis
    - [f] Congenital stenosis or coarctation
  - [2] Extrinsic
    - [a] Intra-abdominal tumors or cysts
    - [b] Aortic aneurysm
    - [c] Hematoma
    - [d] Twisted renal pedicle

2. Adrenal (may be hyperplasia, adenoma, or carcinoma)
   - a] Pheochromocytoma
   - b] Cushing's syndrome
   - c] Primary aldosteronism
   - d] Adrenogenital syndrome (delta -5-pregnanolone block)
3. Miscellaneous
   - a] Coarctation of the aorta
   - b] Toxemia of pregnancy
   - c] Certain brain tumors
   - d] Associated with systemic disease such as porphyria, myxedema, polycythemia, polio, and acromegaly

HISTORY

The author follows a definite pattern in taking a hypertensive history. First, determine when the patient was first told that his blood pressure was elevated and under what circumstances. Second, the patient should be asked how high the blood pressure was at the onset and what the subsequent readings were. It is important that doctors tell their patients the blood pressure readings because it is not uncommon for patients to seek second opinions elsewhere. Third, make note of previous medications used for hypertension, namely, [1] name of drug(s), [2] dosage, [3] duration of use, [4] side effects, and [5] the effect in lowering the blood pressure. Fourth, ascertain if there is a positive family history of hypertension or its complications. A positive family history usually suggests essential hypertension but not invariably so. Fifth, the patient should be carefully screened for historical evidence of secondary hypertension.

For many years, it was felt that hypertension was essential in 95% of cases and secondary in 5% or less. More recently, with the advent of improved diagnostic techniques and curative surgical procedures, Page and associates[2] have estimated that up to 27% of hypertensives have some form of renovascular hypertension. Of late, Conn and associates[3] have gathered circumstantial evidence to support their conviction that 20% of patients with essential hypertension harbor a small, aldosterone-secreting adrenocortical tumor as its cause with cure by removal. This demonstrates the breakthrough that has taken place into the large area of essential hypertension.

THE DIAGNOSIS OF HYPERTENSION

The first step in evaluating a patient with hypertension is to determine if the blood pressure is labile (vascular hyperreactor) or sustained. This often can be difficult and time-consuming. Elevation of both the systolic and diastolic pressures can occur with exertion, fear, anger, and excitement. If the blood pressure is elevated, the patient should be reassured and advised to rest for ten to fifteen minutes in the recumbent position before retaking the blood pressure. It may be necessary to repeat the blood pressure readings two or three times weekly for one to two weeks or longer before deciding if it is labile or sustained. Patients with sustained diastolic hypertension may also have marked lability in their blood pressure readings.

Vascular hyperreactors are usually between the ages of 15 and 35 years; their blood pressures are normal during sleep and in the absence of stress. The patient often tells you that he feels nervous in your office and that his blood pressure in the past was elevated when the doctor took the reading but that it is normal when taken by a nurse, a technician, a mate at home, or at his place of employment. He demonstrates other signs of autonomic overactivity such as a malar flush, sinus tachycardia, and sweaty palms. The blood pressure may or may not return to normal after reassurance and fifteen minutes of rest and it may be very labile during several readings over the course of an hour or two. It may be necessary to sedate the patient for two or three weeks and retake the blood pressure then, but it may or may not return to normal by this method. The cold pressor test is commonly positive in this group of patients.

Once certain of sustained hypertension, the next step is to classify it and determine its severity, that is, whether it is uncomplicated or complicated (see table). This requires a complete history, physical examination, and appropriate laboratory tests.

To screen for renal disease, inquire if the pa-

CRITERIA FOR EVALUATING SEVERITY OF HYPERTENSIVE DISEASE

	Group I	*Group II*	*Group III*	*Group IV*
Symptoms	None or slight (mostly anxiety)	Slight; morning headache, vertigo	Moderate; frequent headaches, fatigue, dyspnea, nocturia	Severe; intense headaches, weakness, confusion, weight loss
Blood pressure	$\frac{150\text{-}200}{95\text{-}105}$	$\frac{150\text{-}200}{100\text{-}110}$	$\frac{180\text{-}250}{110\text{-}140}$	$\frac{240\text{-}300}{140\text{-}180}$
Retina	Normal or minimal arteriolar narrowing	Grade 1 to 2; moderate narrowing and sclerosis, few to moderate focal constrictions	Grade 2 to 3; hemorrhages and exudates	Grade 4; papilledema with or without grade 3 changes
Cardiac function	Normal	Early left ventricular hypertrophy	Left ventricular hypertrophy and congestive heart failure	Left ventricular hypertrophy and congestive heart failure
Renal function	Normal	Normal; occasional slight albumin and casts	Impaired; albumin, casts, red blood cells, blood urea nitrogen elevated	Markedly deteriorated
Central nervous system	Normal	Normal	Cerebrovascular accidents occur	Involved in most cases (encephalopathy)

tient has had flank pain, dysuria, pyuria, hematuria, or albuminuria in the past. Occasionally, there is a family history of polycystic disease.

Pheochromocytoma attacks are suggested by symptoms of sudden headache, nervousness, sweating, pallor, and tachycardia. It should be suspected in patients with any type of spells, thin patients with hypertension, young patients with a short history of hypertension, patients who have features of hypermetabolism but without hyperthyroidism, patients who respond paradoxically to ganglionic blocking agents, patients who become hypertensive during the induction of anesthesia, and patients with hypertension and neurofibromatosis. It should be remembered that 50% of patients with pheochromocytoma have sustained and 50% labile hypertension. Pheochromocytoma attacks may be confused with acute anxiety attacks.

Primary hyperaldosteronism is two and one-half times more common in women than in men. In 70% of cases, the age of patients is between 30 and 50 years. It is associated with symptoms in only a small percentage of cases. These symptoms are polydipsia, polyuria that is mainly nocturia, episodic muscular weakness or paralysis, intermittent tetany or paresthesias, and headaches.

Renovascular hypertension should be suspected in a patient who is young, with a renal bruit; in a patient with recent hypertension and rapid, progressive symptoms; in an older patient or in a patient with chronic, benign essential hypertension with abrupt onset of accelerated hypertension; and in the patient who develops hypertension after abdominal surgery or trauma.

Finally, inquire whether the patient has symptoms of hypertension. These may be mild, moderate, or severe and consist of morning occipital headaches, visual blurring, vertigo, epistaxis, angina, and symptoms of congestive heart failure.

The patient should also be asked about possible licorice or tranylcypromine (Parnate®)[4] ingestion.

PHYSICAL EXAMINATION

A complete physical examination should be done. This may reveal a diagnosis of a systemic disease in which hypertension is part of the symptom complex. Chvostek and Trousseau's signs may be positive in the presence of the alkalosis of florid primary hyperaldosteronism.

The blood pressure should be taken in either the recumbent or sitting position and in both arms. Busy practitioners should at least take the blood pressure in the right, rather than the left, arm in order to detect cases of coarctation of the aorta proximal to the origin of the left subclavian artery.

The hypertensive physical examination should pay special attention to the fundi, heart, and renal areas and the femoral arteries.

The fundi should be classified according to the Keith-Wagener-Barker criteria. Retinal arteriolar narrowing should be graded 1 to 4+; retinal arteriolar sclerosis consisting of silver wires, copper wires, and arteriovenous nicking should also be graded 1 to 4+; focal constrictions should be graded 1 to 4+; and retinopathy such as hemorrhages, exudates, and papilledema should be noted. Funduscopic examination may reveal the duration, severity, and, occasionally, the etiology of the hypertension. The angiospastic fundus is seen in toxemia of pregnancy and in renovascular hypertension. Tortuosity of the retinal arterioles is pronounced in coarctation of the aorta. Using the Keith-Wagener-Barker criteria, the hypertension may be classified from Group (or Grade) 1 to 4. Also, according to the degree of cardiac, renal, and brain damage, the hypertension may be classified from Group 1 to 4. This has resulted in some confusion in the grouping or grading of hypertension (see table).

Cardiac examination should note if there is displacement of the point of maximal impulse, accentuation of the aortic component of the second sound at the base, and the presence of murmurs, gallop rhythm, or signs of congestive failure.

Auscultation of the abdomen should be performed on every hypertensive patient and should be carried out over the costovertebral angles, the lower anterior thoracic area, the epigastrium, and over both renal areas. The diaphragm of the stethoscope is placed approximately 2 in. superolateral to the umbilicus and pressed deep into the abdomen as close to the renal artery areas as possible without causing too much discomfort to the patient. During auscultation, it is best to have the patient hold his breath in expiration. The bruit associated with renal artery stenosis is a high-pitched, continuous sound and is heard in 70% of cases. It can be confused with other causes of abdominal bruits.

Coarctation of the aorta is characterized by a specific murmur. The femoral arterial pulsations should be palpated for their fullness and it should be noted whether they are on time with the radial pulses. It also may be necessary to take the blood pressure in the popliteal spaces. In 20% of cases, coarctation of the aorta occurs at the level of the renal arteries.

LABORATORY INVESTIGATION

In every hypertensive patient, the decision always arises as to how far to go in ordering tests to rule out the secondary causes. This work-up can be costly to the patient. It should be remembered that essential hypertension usually begins after age 40, and, therefore, by and large, all patients under age 40 should have a work-up for secondary causes. In patients between the ages of 40 and 60, the decision to order a secondary work-up may depend on the findings during the history and physical examination, one's past experience with hypertension, and, often, intuition. In patients over the age of 60 or 65, there is generally less morbidity from hypertension. The decision is again based on the same criteria as the previous group. Acceleration of hypertension of recent onset or of a chronic benign form should indicate the need to study the older patient more fully.

A work-up to rule out the secondary causes of hypertension usually includes a complete blood count, routine urinalysis, blood urea nitrogen, serum potassium, chest X-ray, 12-lead electrocardiogram, intravenous pyelogram, and twenty-four-hour urine test for catecholamines.

Pheochromocytoma. In pheochromocytoma, the blood sugar and the basal metabolic rate are commonly elevated, while the serum protein-bound iodine is normal. The twenty-four-hour urine test for catecholamines generally has been a poor screening test. Urinary vanillomandelic acid is a more reliable test but also has not lived up to expectations. Urinary metanephrines are the most reliable, with the lowest incidence of false-negatives. A phentolamine (Regitine®) test for sustained hypertension and a histamine-cold pressor test for labile hypertension, employing measurements of the blood pressor amines at appropriate times during the tests, may be most helpful in confirming the diagnosis.[5]

Renovascular hypertension. Renovascular hypertension is the most common cause of potentially reversible hypertension. The timed, intravenous pyelogram, isotope renogram, renal arteriogram, and renal split-function studies may be used consecutively for diagnostic purposes. Abnormal intravenous pyelograms may demonstrate one of several findings.[6] There may be absolutely no function on one side, as in renal artery thrombosis. There may be delay in appearance and greater or lesser concentration of contrast medium on the affected side. The affected kidney may be smaller than the normal one, a difference of 1.5 cm. or more being significant. The isotope renogram correlates with the para-amino hippurate clearance and the measurement of urine flow. It often confirms and may add information not obtainable from the intravenous pyelogram. The curves for each kidney represent a vascular, parenchymal, and outflow index. At times, the renogram may be confusing and variable according to the patient's hydration, cooperation, and recumbent or upright position during the test.[7]

Transfemoral aortography, as described by Seldinger,[8] provides a tool for precise anatomical and pathological diagnosis of renovascular abnormalities. It has become evident that the mere demonstration of a lesion on aortography is not sufficient to incriminate the abnormality as a cause of hypertension in a given patient.

Differential renal function studies, as designed by Stamey,[9] can serve as a definitive diagnostic tool for evaluating the functional significance of a radiographically demonstrated lesion and for providing information upon which one can base a reliable prediction on the outcome of corrective surgery. Split-function studies are necessary in the presence of bilateral renovascular disease and require bilateral ureteral catheterization. Para-amino hippurate and inulin clearances from each kidney are calculated as a mean of 3 consecutive ten-minute collection periods. Sodium and potassium excretion, urine osmolarity, and urine volume and flow can also be determined from each kidney.

Primary hyperaldosteronism. Primary hyperaldosteronism features low-serum potassium, normal or increased serum sodium, metabolic alkalosis, urine of low specific gravity that is neutral or alkaline, increased body-exchangeable potassium, impaired glucose tolerance in 50% of cases, and increased urinary potassium and aldosterone. Because of the infrequency of symptoms, the classic triad has been hypertension, low serum-potassium, and increased urinary aldosterone. If the patient has been on thiazide diuretics, it will be necessary to discontinue their use for four to six weeks before redetermining the serum potassium.

More recently, Conn and associates[3] have described a case of normokalemic primary hyperaldosteronism. Thus, the triad has been changed to hypertension, decreased plasma renin, and increased urinary aldosterone. Unfortunately, the measurement of plasma renin is a bioassay and is not yet available in most laboratories.

Coarctation of the aorta. If coarctation of the aorta is suspected and the femoral arterial pulsations are equivocal, a simple procedure is to place needles in both the radial and femoral arteries for comparison of pressure readings and pulse curves. Aortography is the final procedure in localizing the site of coarctation.

TREATMENT OF HYPERTENSION

Approximately 90% of patients with essential hypertension can be treated on an outpatient basis. All treatment begins with the basic measures of reassurance, more relaxation, and correction of obesity. Moderation in such things as salt intake, coffee, and cigarettes is always the important rule.

Systolic hypertension. A systolic blood pressure of over 150 mm. Hg and, for that matter, over 200 mm. Hg, requires no treatment, and the patient should not be told he has hypertension. This is most commonly due to atherosclerosis.

Vascular hyperreactors. Vascular hyperreactors may need mild sedation. They should be advised to have examinations at least once yearly because of the higher incidence of future essential hypertension in this group.

Renovascular hypertension. Medical therapy may be indicated and is often adequate in certain cases of stenotic renovascular lesions. Some of the indications for medical therapy are [1] bilateral disease of the renal vessels involving both the primary and secondary branches, [2] unilateral disease of the primary or secondary branches when surgery is not feasible, [3] patients over age 60, and [4] patients 40 years of age or more in whom the blood pressure is adequately controlled with medications. In certain cases of stenotic renal artery lesions, the lesion may progressively worsen despite good medical control of the blood pressure. The indications for surgery in renovascular hypertension include [1] the failure to respond to medical therapy, [2] the refusal of adequate medical therapy, [3] patients 40 years of age or less with unilateral lesions or with bilateral disease confined to the main renal arteries (two-stage procedure), and [4] the progressive deterioration of renal function.[10]

Essential hypertension. Most physicians feel that therapy is indicated in early uncomplicated essential hypertension to forestall progressive vascular damage. The intensity of treatment depends on the degree of vascular impairment rather than the blood pressure reading at any given instant. The patient should have a thorough understanding of the principles involved in order to gain his confidence and cooperation, and he should be told why hypertension is treated. He also should be informed of the following facts: [1] medications must be taken daily for an indefinite period of time; [2] once blood pressure is controlled, blood pressure checks every two to three months and a complete examination once yearly will be necessary; [3] how the antihypertensive drug works and its possible side effects; [4] a repeat intravenous pyelogram or isotope renogram may have to be done periodically to recheck for renovascular hypertension; [5] purchase of a sphygmomanometer to take his own blood pressure and adjust his own medications may be required; and [6] antihypertensive drugs and periodic blood pressure checks can be costly.

Antihypertensive drugs should be individualized for each patient. The practitioner should become familiar with and use only a few drugs.

The author uses only three drugs to treat mild to moderate hypertension. These are hydrochlorthiazide (HydroDIURIL®), hydralazine (Apresoline®), and guanethidine (Ismelin®). Combination antihypertensive drugs are not used; thus, adjustments in dosage are made easier.

HydroDIURIL®[11] acts on the renal tubules causing a diuresis by interfering with sodium resorption, thus lowering plasma volume. It also lowers blood pressure by reducing the peripheral resistance. Noteworthy side effects are a hyperglycemic effect, hyperuricemia with gout, and hypokalemia. Apresoline®[12] has a direct spasmolytic effect on blood vessels. Noteworthy side effects are orthostatic hypotension, tachycardia, headaches, angina, depression, and systemic lupus erythematosus. Ismelin®[13] has a selective sympathetic inhibition and acts by depleting catecholamines from peripheral nerve endings in blood vessels. Side effects are due to the unopposed parasympathetic activity and may be nasal stuffiness, diarrhea, orthostatic hypotension, inhibition of ejaculation, frequency of urination, weakness, and depression.

In the average patient, therapy is started with HydroDIURIL®, 50 mg. twice daily, and the patient is asked to return in two weeks for a blood pressure reading. Ideally, the patient should return and have the blood pressure checked by a nurse or technician at 8:00 A.M., noon, and 3:00 P.M., carrying on his usual daily routine between checks. The doctor should see the patient at 4:00 P.M. and check the blood pressure. In this way, the variation in blood pressure through the day can be appreciated and sometimes the medications are adjusted accordingly. HydroDIURIL® can be expected to lower the blood pressure as much as 25 mm. Hg systolic and 10 mm. Hg diastolic in two weeks. If the diastolic pressure is not 90 mm. Hg or less at that time, Apresoline® or Ismelin® is added to the program. Generally speaking, if the patient is not subject to headaches and does not have angina, Apresoline® is started in a dose of 10 mg., four times daily. The blood pressure is then checked at two-week intervals and the Apresoline® may be increased to 25 mg. four times daily and to a maximum of 50 mg. four times daily to achieve control with a minimum of side effects. If the patient has frequent headaches or angina or, from the standpoint of convenience of administration, Ismelin® is used instead of Apresoline®. For convenience, the entire dosage may be given at bedtime, starting with 10 mg., increasing to 25, 50, 75, 100, and up to 200 mg. after suitable intervals. By giving it at bedtime, orthostatic hypotension may be minimized. Patients on Ismelin® should have blood pressure checked in both recumbent and upright positions.

Occasionally, all three medications are used in a severe Group 2 or Group 3 hypertension.

The patient on HydroDIURIL® should be advised to have a large glass of orange juice daily for potassium. Serum potassium and blood urea nitrogen should always be checked at three- to four-month intervals. Approximately 25% of hypertensive patients treated with thiazides develop significant hypokalemia. Conn suspects that these patients probably have primary aldosteronism. Enteric-coated potassium chloride, either alone or combined with a thiazide diuretic, should be avoided because of the small risk of inducing small bowel ulceration. If supplemental potassium is necessary, Potassium Triplex or elemental potassium (Kaon®) may be used in a dosage of 1 to 3 tbsp. daily.

Patients with hypertension and intermittent or progressing cerebrovascular insufficiency should have the diastolic pressure lowered to between 95 and 100 mm. Hg. If lowered below 95 mm. Hg, there is an increased risk of cerebral thrombosis. If anticoagulant therapy is indicated in such a patient, lowering of the diastolic pressure below 110 mm. Hg reduces the risk of cerebral hemorrhage.

In the presence of hypertension with mild to moderate renal insufficiency, alpha methyldopa (Aldomet®) is the drug of choice.[14] The dose is gradually increased to 1 gm. daily in the first week, with subsequent weekly increments of 500 to 750 mg., until the dose is limited by side effects, adequate blood pressure response, or reaches a maximum of 3 gm. daily.

Malignant (accelerated) hypertension. Some patients with Group 3 and all patients with Group 4 (malignant) hypertension require hospitalization for control of the blood pressure. Reserpine, in doses of 2.5 to 5 mg. intramuscularly every six to eight hours, may be used. For Group 4, hypertension featuring papilledema, severe symptoms (for example, encephalopathy), renal failure, and blood pressures of over 250/140, the drug of choice is sodium nitroprusside, 60 mg. per liter; the initial rate should not be greater than 10 drops per minute; the rate should be increased 5 drops per minute every five minutes until the blood pressure is brought to approximately 150/100. The blood pressure is then maintained at this level and Aldomet® and/or Apresoline® are started to take over the control from the sodium nitroprusside.

PREOPERATIVE AND POSTOPERATIVE CARE OF PATIENTS WITH HYPERTENSION

Patients with uncomplicated hypertension tolerate surgery well. In Smithwick's series of sympathectomies for hypertension, the mortality rate was 1% in uncomplicated hypertension and 10% in the presence of papilledema.[15] The preoperative renal status is important and those with azotemia (blood urea nitrogen over 50 mg. percent) tolerate surgery poorly. Congestive failure secondary to hypertension should be under optimal control preoperatively.

It is most important to rule out pheochromocytoma before surgery because of the risk of hypertension during the induction of anesthesia, with possible subsequent stroke, arrythmias, and heart failure.

Mild to moderate essential hypertension is lowered nonspecifically for two to four weeks postoperatively. Severe hypertension is unchanged.

Ganglionic blocking agents, Apresoline®, and thiazide diuretics all have a short duration of action and should be stopped one to two days preoperatively. A patient with hypertension who is on digitalis and thiazides preoperatively should have serum potassium checked. Low serum potassium potentiates digitalis and may result in arrhythmias. Ismelin®, which depletes tissue catecholamines, should be discontinued two weeks preoperatively and ganglionic blocking agents substituted so that blood pressure control is not lost; these can be stopped one to two days before surgery. Rauwolfia products which lower tissue catecholamines should also be stopped two weeks preoperatively. If this is not done, there is the risk of hypotension and bradycardia during anesthesia.

Postoperatively, hypertension control is individualistic and one cannot generalize. Most patients with mild to moderate hypertension require no medication for two to four weeks, until the blood pressure regains the preoperative levels.

The management of pheochromocytoma during surgery can be difficult. To offset the sharp rise in blood pressure during the induction of anesthesia, in intravenous infusion of 1,000 ml. 5% glucose in water containing 5 mg. of phentolamine hydrochloride (Regitine®) is used. During removal of the tumor, the blood pressure usually falls precipitously so that an intravenous levarterenol (Levophed®) drip or a blood transfusion is necessary.

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RADICAL SURGICAL ATTACK can result in a cure rate of more than 50% in previously untreated cancer of the vulva. Single-stage radical vulvectomy under local anesthesia usually is possible despite advanced age and associated malignant conditions and complicating disease. Operative mortality is not prohibitive and almost always is the result of lesions unrelated to the vulvar carcinoma or to the surgery directly, and significant complications are uncommon. Pelvic lymphadenectomy increases operative risk and should be considered only when Cloquet's lymph node or external iliac lymph nodes contain tumor. Clinical staging indicates individual prognosis and aids in evaluation of therapy. Observations are based on study of 148 women with cancer of the vulva.

JOHN L. MC KELVEY, M.D., and LEON L. ADCOCK, M.D., University of Minnesota, Minneapolis. Cancer of the vulva. Obstet. and Gynec. 26:455-466, 1965.

Paroxysmal Atrial Flutter in Wolff-Parkinson-White Syndrome

1 to 1 Atrioventricular Conduction Resembling Ventricular Tachycardia

KOO YOUNG CHUNG, M.D., and JOHN THOMAS, M.D.

Nashville

THE OCCURRENCE OF various cardiac arrhythmias in subjects with the Wolff-Parkinson-White syndrome is well known. The most common forms of such arrhythmias are paroxysmal atrial tachycardia and atrioventricular nodal tachycardia; atrial fibrillation or flutter is less common.[1–4] In general, the occurrence of atrial flutter with 1 to 1 atrioventricular conduction is a rare phenomenon, however, it may appear in some forms of heart diseases.[4] As far as can be ascertained, it has never been reported in a patient with Wolff-Parkinson-White syndrome.

The purpose of this paper is to report a very rare occurrence of atrial flutter with 1 to 1 atrioventricular conduction resembling ventricular tachycardia in a patient with Wolff-Parkinson-White syndrome, and to call attention to the value of electroconversion therapy.

CASE HISTORY

A 64-year-old male with hypertension of five years' duration was admitted to the George W. Hubbard Hospital of Meharry Medical College, because of rapid heart action accompanied by dyspnea and profuse perspiration of seven hours' duration. On the day of admission, while having breakfast, the patient experienced a sudden onset of rapid palpitation. He gave a history of a similar episode approximately five years previously. Another also occurred, for a brief period, three weeks before this hospitalization but stopped spontaneously. There was a denial of chest pain, nausea, and vomiting. He had not taken any antihypertensive medication or digitalis preparation for at least five years.

The significant physical findings were: blood pressure 170/110 mm. Hg, irregular tachycardia 130 to 260 beats per minute, and moderate left ventricular hypertrophy with bilateral basal pulmonary rales. The blood chemistry was normal except for a serum transaminase of 55 units.

The electrocardiogram, taken immediately after admission, was initially interpreted as atrial tachycardia with intermittent ventricular tachycardia (Figure 1A) by the house staff. Carotid sinus pressure was not effective in terminating the arrhythmia. Digoxin, 1 mg., was administered intramuscularly without any benefit and an additional 0.5 mg., given four hours later, was also ineffective. A review of the electrocardiogram revealed the arrhythmia to be atrial flutter with 2 to 1 atrioventricular conduction and intermittent 1 to 1 atrioventricular conduction with marked aberrant ventricular conduction. After other measures failed external electric The rhythm immediately became of sinus mechanism countershock with 100 watt-seconds was administered. with associated atrial parasystole (Figure 3B). There was now evident Wolff-Parkinson-White syndrome, type B (Figure 4). Quinidine, 0.4 gm., every six hours orally, was given in addition to continuing digitalis therapy. The patient felt fine and had sinus rhythm until twelve hours after admission when he suddenly became rigid and extended his neck and extremities. No vital signs were obtainable. All attempts at resuscitation failed. Postmortem examination did not reveal myocardial infarction or any other cardiac abnormality except for moderate left ventricular hypertrophy. The cardiac conduction system was not examined.

ELECTROCARDIOGRAPHIC ANALYSIS

Figure 1A was taken immediately after admission and Figure 1B was taken one hour after admission. Both A and B show atrial flutter with a rate of 260 per minute. This electrocardiogram can be interpreted as atrial flutter because the atrial rate is faster than 250 per minute. The atrial wave resembles a retrograde P wave simply due to the fact that only the lower edge of the flutter wave is clearly seen. The possibility of atrioventricular nodal tachycardia with 2 to 1 antegrade atrioventricular conduction (Figure 1B) can be excluded because atrioventricular nodal tachycardia usually produces a rate slower than 250 per minute, which, on the other hand, is characteristic of atrial flutter.[1,4] A 1 to 1 atrioventricular conduction with such a fast rate is more prone to occur in atrial flutter than a 1 to 1 A-V conduction in A-V nodal tachycardia because the retrograde conduction

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KOO YOUNG CHUNG *is assistant professor of medicine, assistant director of Heart Station, and associate investigator, and* JOHN THOMAS *is professor and director of Heart Station, Department of Medicine, and director of Cardiovascular Disease Clinical Research Program Project, Meharry Medical College, Nashville.*

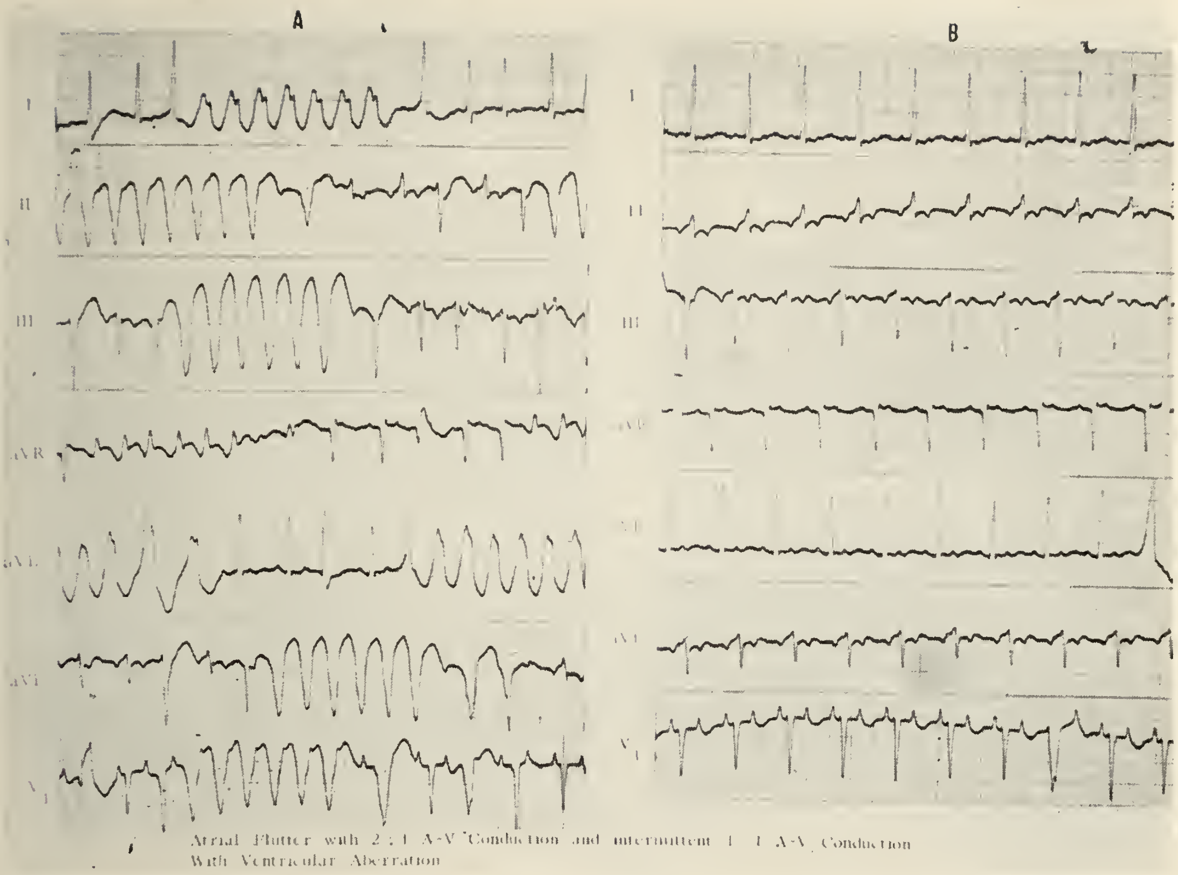

A
B
I
II
III
aVR
aVL
aVF
V1
Atrial Flutter with 2 : 1 A-V Conduction and intermittent 1 : 1 A-V Conduction
With Ventricular Aberration

Fig. 1. (A.) Atrial flutter with 2 to 1 atrioventricular conduction and intermittent 1 to 1 atrioventricular conduction with ventricular aberration. (B.) Atrial flutter with 2 to 1 atrioventricular conduction and occasional ventricular premature beats. Atrial rate is 260 per minute.

in the A-V junctional tissues is physiologically handicapped more than in antegrade conduction, during a rapid tachycardia.[4] Another possibility of atrial tachycardia with 2 to 1 atrioventricular conduction may be considered because a typical "sawtooth" pattern of atrial flutter wave is not seen. Also, rarely, the P wave may be conducted in retrograde fashion in atrial tachycardia if the ectopic focus is located in the atria very near the atrioventricular node. However, the atrial rate of 260 per minute with rare retrograde conduction in atrial tachycardia is unlikely.

Figure 1B exhibits atrial flutter, with 2 to 1 atrioventricular conduction and occasional ventricular premature contractions throughout the tracing. Figure 1A represents atrial flutter with intermittent 1 to 1 and 2 to 1 atrioventricular conduction. The QRS complex during 2 to 1 atrioventricular conduction and 1 to 1 atrioventricular conduction are completely different. The QRS complex during 1 to 1 atrioventricular conduction is almost the same configuration as the QRS complex in Figure 2, which was taken two hours after admission. Figure 2 represents atrial flutter with 2 to 1 atrioventricular conduction and marked aberrant ventricular conduction of the left bundle branch block pattern. The bizarre and wide QRS complex in this tracing is probably resulting from the marked slurring of the upstroke of the QRS complex due to a delta wave and left bundle branch block (either true coexisting anatomical block or functional block due to the rapid heart rate). Flutter waves are not clearly seen in Figure 2 because every other wave is superimposed on the QRS complex. The diagnosis of atrial flutter with 2 to 1 atrioventricular conduction can be made because the R-R intervals in Figure 1B and Figure 2 are precisely equal and the configuration of the flutter waves in lead V_1 is exactly the same.

In Figure 1A, some portion of the tracing during 1 to 1 atrioventricular conduction very much resembles ventricular tachycardia. This can be excluded on the basis of the precisely equal R-R interval during 1 to 1 atrioventricular conduction in Figure 1A to atrial flutter cycle and the same

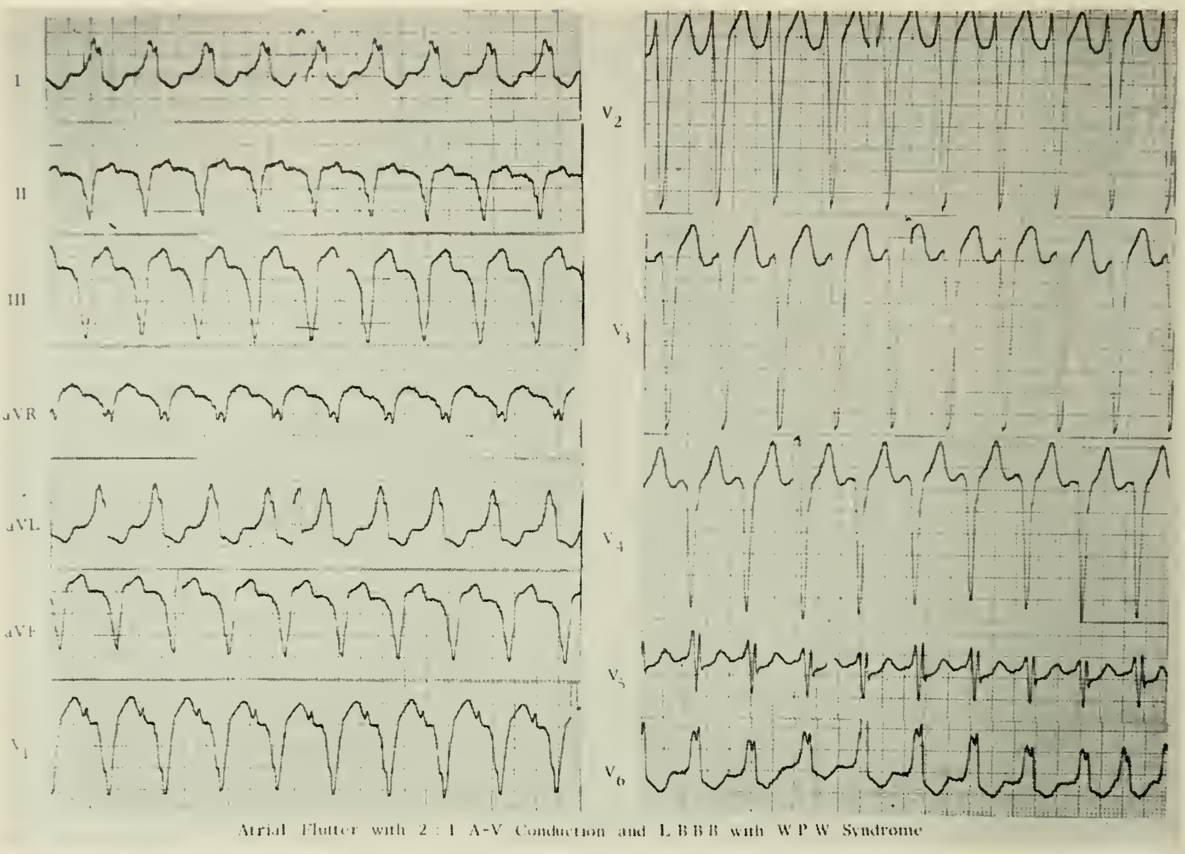

I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6
Atrial Flutter with 2 : 1 A-V Conduction and L B B B with W P W Syndrome

Fig. 2. Atrial flutter with 2 to 1 atrioventricular conduction. Every other flutter wave is superimposed to QRS complexes. Markedly prolonged QRS complex (0.20 second) is due to a delta wave and left bundle branch block. Note similar QRS complex between Figure 1A during 1 to 1 atrioventricular conduction and Figure 2.

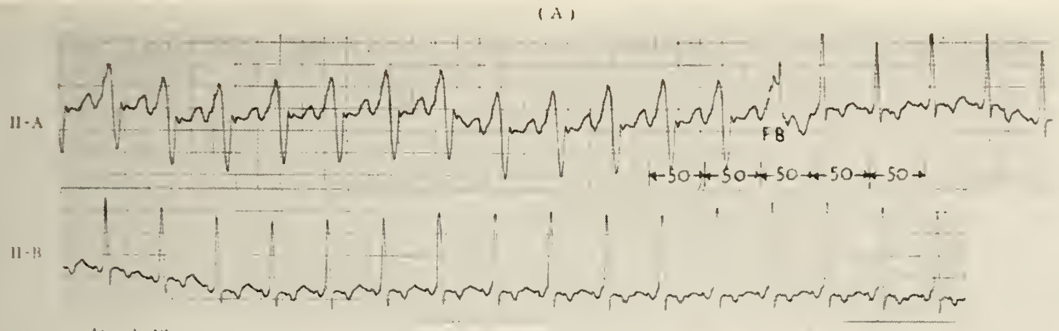
QRS complex configuration between Figure 1A and Figure 2.

Figure 3A was taken approximately five hours after admission, and lead II A and B is continuous. The tracing shows atrial flutter with 2 to 1 atrioventricular conduction and aberrant ventricular conduction. The flutter cycle is measurable throughout the tracing and the R-R interval (0.50 second) is precisely the same as the R-R interval in Figure 1B and Figure 2 which indicates that the tracing shows atrial flutter with 2 to 1 atrioventricular conduction. It is very interesting to note that there are 2 types of QRS complexes without changing any R-R interval (the interval from the beginning of QRS complex to the beginning of QRS complex of the following beat) or flutter cycle, and there is 1 ventricular fusion beat (marked as FB). It can be assumed that there may be 2 accessory pathways by judging the 2 anomalous atrioventricular conduction pathways, since both types of QRS complex exhibit a delta wave. Also, the existence of the ventricular fusion beat without a changing R-R interval strongly suggests the presence of 2 different anomalous pathways. The QRS complexes in lead II, A of Figure 3A, resemble the QRS complex in Figure 4 but the former shows more bizarre and wider QRS configuration.

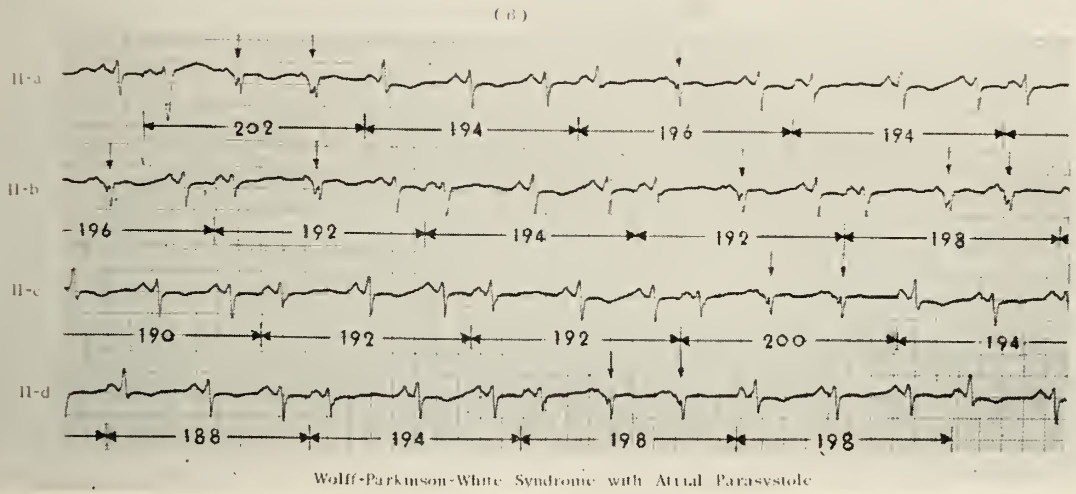
Figure 3B was taken immediately after application of external electric countershock. Lead II (a, b, c, d) is continuous. This tracing reveals a normal sinus rhythm with atrial parasystole and intermittent aberrant ventricular conduction following the parasystolic beats (arrows). The QRS complex of the aberrantly conducted beats is preceded by a wide and notched P wave. This P wave change probably represents aberrant intraatrial conduction which may occur following atrial premature beats or atrial parasytolic beats.[5,6] This type of conduction has been observed by different authors and discussed in previous papers in detail.[5] These bizarre P waves and QRS complexes may represent an ectopic atrial focus with an anomalous pathway because of the short P-R interval with the delta wave.

The diagnosis of atrial parasystole was made because of varying coupling intervals and fixed interectopic intervals according to diagnostic criteria for parasystole discussed previously.[5,7,8]

Figure 4 is the complete tracing during sinus



Atrial Flutter with 2 : 1 A-V Conduction and 2 kinds of QRS complexes in W-P-W Syndrome



Wolff-Parkinson-White Syndrome with Atrial Parasystole

Fig. 3. (A.) Lead II-A and B is continuous. The rhythm is atrial flutter with 2 to 1 atrioventricular conduction. The atrial rate is 260 per minute which is the same as in Figure 1A and B and Figure 2. There are 2 kinds of QRS complexes and both types exhibit delta waves which indicate 2 anomalous pathways. Note 1 ventricular fusion beat (marked as FB). R-R interval is precisely regular throughout. (B.) Lead II a, b, c, and d are continuous. The rhythm is sinus mechanism with atrial parasystole. The sinus rate is 90 and the parasystolic rate is 32 per minute. Note aberrantly conducted beats (arrows).

mechanism with a rate of 95 per minute. This tracing demonstrates a typical Wolff-Parkinson-White syndrome, type B.[9] Delta waves are best seen in leads I, III, aVR, aVL, and V_{1-4}. The P-R interval is 0.08 second and the QRS interval is 0.11 second by using the best leads which demonstrates all features of anomalous atrioventricular conduction (leads I and aVL). This tracing also reveals evidence of left ventricular hypertrophy and occasional ventricular and atrial ectopic beats.

DISCUSSION

Wolff-Parkinson-White syndrome was first recognized as a clinical entity in 1930.[3] It has been considered as a benign syndrome as there are no subjective manifestations or hemodynamic disturbances resulting from ventricular preexcitation itself.[9] However, paroxysmal rapid heart action, which tends to be associated with this condition, frequently requires urgent medical attention.[1–4,10–16] Sudden death during or after episodes of tachycardia has been reported.[9,17–19] The paroxysm itself may frequently cause congestive heart failure[20–22] and sometimes irreversible changes in the heart.[23]

Wedd[24] first called attention to the occurrence of paroxysmal rapid heart action in this syndrome in 1921. The incidence of tachycardia varies between 40 to 80% as reported by many different authors.[1–4,9,12,16,18,25] The type of tachycardia in the Wolff-Parkinson-White syndrome is a rapid, regular, supraventricular tachycardia in the majority of cases.[1–4,11,13,16] Atrial fibrillation and atrial flutter are rather uncommon in the Wolff-Parkinson-White syndrome.[1–4,11–13,26–29] Atrial flutter is far more rarely encountered than atrial fibrillation.[1,2,4,11,13] If atrial fibrillation or flutter occurs in Wolff-Parkinson-White syndrome, it has been frequently found in patients with associated rheumatic heart disease.[1,2,4,30] Only 4 cases of atrial fibrillation and 1 of atrial flutter among 40 instances of Wolff-Parkinson-

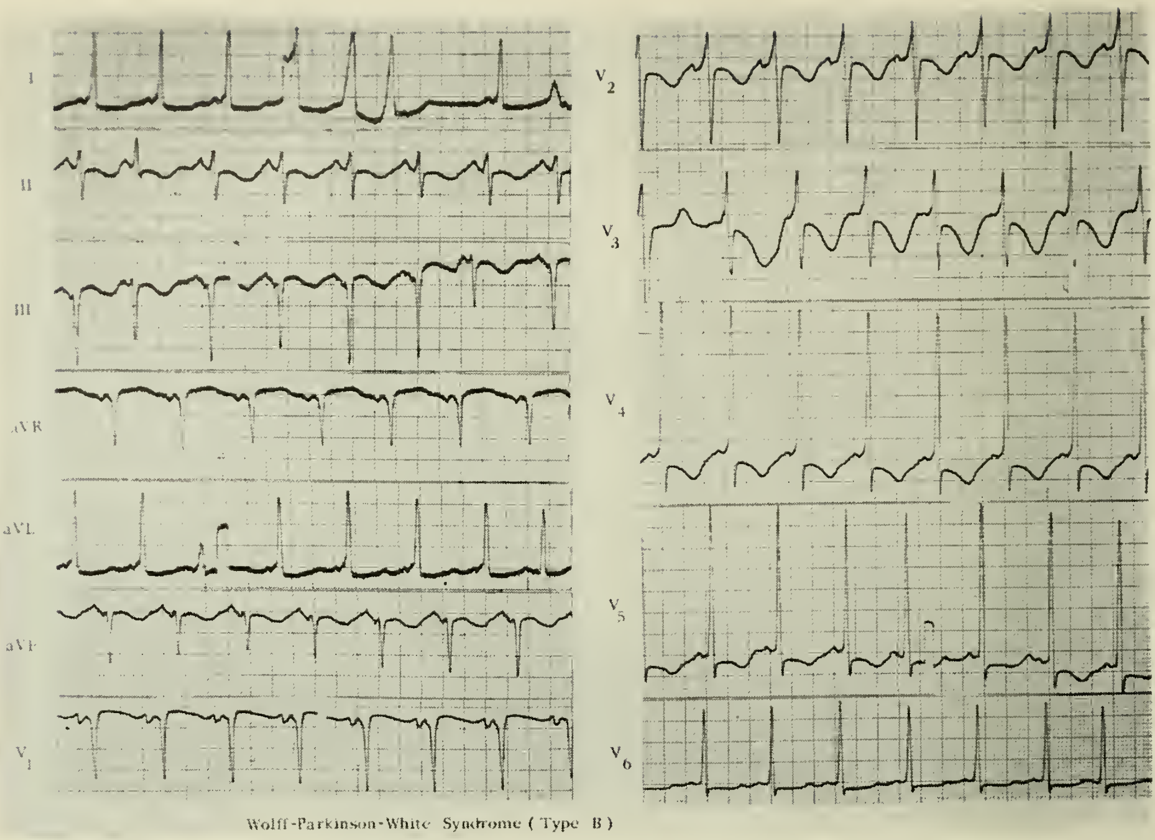


Fig. 4. Wolff-Parkinson-White syndrome, type B

White syndrome were found in a previous study.[2] They all occurred in type A.

It is noteworthy that the present patient has type B Wolff-Parkinson-White syndrome during sinus rhythm, although the possibility of multiple accessory pathways is raised since more than 1 type of QRS complex is noted. This finding suggests that both types A and B Wolff-Parkinson-White syndrome might exist in this patient. The occurrence of more than 1 type of abnormal ventricular complex in different paroxysms of rapid heart action has been observed previously.[2,10–13,19] and is best shown in Figure 3A.

The QRS complex during paroxysmal tachycardia in Wolff-Parkinson-White syndrome is normal in the majority of cases of regular supraventricular tachycardia.[1,2,4,19,26,31,32] However, atrial fibrillation or flutter associated with Wolff-Parkinson-White syndrome frequently exhibits abnormally wide QRS complexes either due to anomalous atrioventricular conduction via accessory pathway or ordinary aberrant ventricular conduction resulting from a rapid rate.[1,4,30] In this situation, the QRS deflection may simulate ventricular tachycardia[1,4,11,26,33] as seen in Figure 1A. Scherf and Schonbrunner[26] were the first to note occurrence of wide QRS complexes during paroxysmal atrial fibrillation or flutter.

Although the occurrence of ventricular tachycardia in Wolff-Parkinson-White syndrome has been reported by several observers,[26,34–38] the authors have been unable to find a single unequivocal case of the arrhythmia in Wolff-Parkinson-White syndrome. The most likely diagnosis of such arrhythmias in the cases reviewed was a rapid atrial fibrillation or flutter with wide QRS complexes.

There are different theories regarding the mechanism of the Wolff-Parkinson-White syndrome and the occurrence of various arrhythmias in this syndrome. The most acceptable theory at the present time suggests conduction over an accessory pathway.[1,2,4,9–13,38–42] This theory has been supported by experimental studies[9,12,31] and clinically by autopsy finding.[9,11,31,43,44]

With regard to the mechanism proposed for the rapid ectopic tachycardias occurring in the Wolff-Parkinson-White syndrome, the reentry phenomenon has been postulated by different authors.[1,2,4,11,13] In paroxysmal atrial tachycardia and atrioventricular nodal tachycardia, a paroxysm of rapid heart action may be precipitated by passage of the ectopic atrial or atrioventricular nodal impulses downward through the atrioventricular node and its subsequent return to the atria or atrioventricular node via the accessory pathway, thus constituting a form of reentry.[1,2,4] The paroxysmal tachycardia will persist if the reentry phenomenon is repetitive. In paroxysmal atrial fibrillation or flutter, the above mentioned reentry phenomenon alone is not satisfactory to explain the mechanism since a seemingly impossibly high ventricular rate would have to be assumed. However, some investigators[1,4,13,30] have postulated the mechanism initiating the paroxysm may be reentry but that the impulse is returned to the atria very early. If it arrives during the "vulnerable" period of the atria, the reentry impulse may cause the onset of atrial fibrillation or flutter.[1,4,13,30] During these arrhythmias, a rapid, almost constant, stream of atrial impulses passes down either the accessory bundle or the atrioventricular node and bundle branch system, depending upon which is less refractory at the time of onset of the rapid heart action.

The correct diagnosis of Wolff-Parkinson-White syndrome during an episode of rapid heart action is often difficult and sometimes impossible without comparing the tracing during sinus mechanism. Some investigators[45,46] pointed out that very rapid heart action associated with abnormal QRS complexes is suggestive of Wolff-Parkinson-White syndrome, especially if a supraventricular origin of the tachycardia can be demonstrated. In addition, atrial fibrillation or flutter with rapid ventricular rate is not influenced by digitalis should arouse the suspicion of an underlying Wolff-Parkinson-White syndrome[47] since the digitalis is capable of prolonging or completely blocking conduction in the normal A-V pathway.[11,30] The case presented demonstrates a good example of such a situation since the rapid heart action did not respond to a fairly large amount of parenteral administration of digitalis (1.5 mg. of digoxin). Quinidine or procainamide is highly capable of depressing conduction via the accessory pathway and as a result, the preexcitation QRS complexes disappear following administration of such drugs. It appears that best results are achieved by giving digitalis and quinidine or procainamide simultaneously for paroxysmal rapid heart action in the Wolff-Parkinson-White syndrome, particularly, in atrial fibrillation or flutter.[1,2,4,13,30]

External electric countershock has been employed for treatment of various rapid cardiac arrhythmias. Fisch and associates[48] have used this successfully for supraventricular tachycardia associated with Wolff-Parkinson-White syndrome. The present patient also responded promptly to electric countershock initially, although he died suddenly the next day.

The coexistence of ventricular parasystole and Wolff-Parkinson-White syndrome has been rarely observed previously.[2,4,9,18,49,50] The first case of atrial parasystole associated with Wolff-Parkinson-White syndrome was reported in a previous paper[2] and the present case is probably the second reported instance of such an arrhythmia. Ventricular parasystole, in general, occurs once in 900 to 1,200 routine electrocardiograms taken in a general hospital,[5,7,8] while the Wolff-Parkinson-White syndrome has an incidence of 0.15 to 0.2%.[2,4,18,49,51,52] Therefore, the combination of parasystole and the Wolff-Parkinson-White syndrome is very rare.

The coexistence of Wolff-Parkinson-White syndrome and left bundle branch block has been reported previously.[53,54] This combination, in itself, is rare. Also, sometimes left bundle branch block cannot be diagnosed because Wolff-Parkinson-White syndrome may obscure the electrocardiographic pattern if the chamber with the interrupted bundle is activated prematurely.[53] Figure 2 of this case represents a combination of Wolff-Parkinson-White syndrome and left bundle branch block because the terminal portion of the QRS complexes is typically left bundle branch block in addition to a characteristic Wolff-Parkinson-White syndrome complex. This left bundle branch block is more than likely on an anatomical rather than a functional basis, since the ventricular rate is not fast enough to cause ordinary ventricular aberration.

SUMMARY

An instance of the rare occurrence of atrial flutter with 1 to 1 atrioventricular conduction resembling ventricular tachycardia in Wolff-Parkinson-White syndrome is presented. This is the first reported case as far as the authors can ascertain.

The rare combination of atrial parasystole following conversion to sinus rhythm and a left bundle branch block during paroxysm existed.

The importance of the correct diagnosis of the rapid heart action in Wolff-Parkinson-White syndrome is emphasized in relation to treatment. The drug therapy of choice for atrial fibrillation or flutter associated with Wolff-Parkinson-White syndrome is a combination of digitalis and quinidine or procainamide. External electric countershock effectively converted the paroxysm to sinus rhythm after other methods failed.

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Series on ALLERGY *for the* PRACTITIONER

Environmental Control in the Treatment of Allergic Individuals

LLOYD S. NELSON, M.D.
Minneapolis

The airborne contaminants cover a wide range of particle sizes from large visible particles of approximately 15 μ in diameter to submicroscopic viruses. Particle size is important in considering air cleaning devices, and the first plate (Fig. 1) illustrates the type of air contamination in our surroundings. Dust particles vary in size. Ninety percent of the weight of a typical dust sample taken from ordinary air is concentrated in those particles over 5 μ in diameter. More than 90% of the particles by count are those below 5 μ in diameter; an estimated 90% of the dust particles are less than 0.01 μ in size. It is clearly obvious that when a filter claims to be 90% efficient, it means absolutely nothing in reference to dust cleaning efficiency. When speaking of a given type of pollen in which the particle size is fairly uniform, the percentage by weight and by count is somewhat closer.

The simplest method of reducing the airborne contaminant level is to use some type of filtering mechanism. A common filter on the market is the viscous impingement (Fig. 2) or ordinary fiber filter which consists of randomly oriented fibers of various materials, usually of spun glass consistency, arranged so that the open spaces are much larger than the diameter of the particles to be removed. The filtering action depends upon the particles contacting and adhering to the fibers or collecting surface as the air flows and twists through the filter structure. The inertia of the heavier particles carries some of them on to the media surfaces. The smaller particles are not trapped because of their high surface to weight ratio, and this keeps them in the airstream. This filter is called a "roughing filter" and is used in the majority of forced air systems in homes today. This filter has a low particle-removing efficiency—about 5 to 7% by the National Bureau of Standards' Dust-Spot Method. It stops some of the large particles but is of little value on particles smaller than 5 μ.

There are two roughing filters generally available, namely viscous-coated and dry. In the viscous type, the fibers are coated with an adhesive substance, usually an oil, which aids in trapping the particles. Some of these filters are constructed for indefinite use and can be cleaned and reoiled when the filters become loaded. The dry type (Fig. 3) of roughing filter is composed of loosely packed glass or other fibers, cotton batting, or paper. In general, it offers more resistance to the passage of air and has a little higher filtration efficiency than the viscous type. Dry filters cannot be recleaned and must be discarded. This filter is designed to strain the air and is 30 to 95% efficient but has two important disadvantages. First, it is costly and must be replaced when loaded with dirt. Second, and more serious, the tightly packed construction of this filter causes an evident pressure drop and as with all mechanical filters, dirt accumulates in the first few inches of the filter causing added pressure drop and thereby reducing the efficiency of the unit. A larger fan than is usually found in most furnaces is needed to force air through this kind of filter.

A third kind of filter is the self-charging electrostatic type (Fig. 4). It is constructed of plastic fibers which have random position and negative charges over its surfaces. These charges attract and collect particles. Efficiency is low. It loads up quickly and its effectiveness decreases with a rise in humidity.

The charged medium electrostatic filter (Fig.

LLOYD S. NELSON *is a member of the Clinical Staff, University of Minnesota Medical School.*

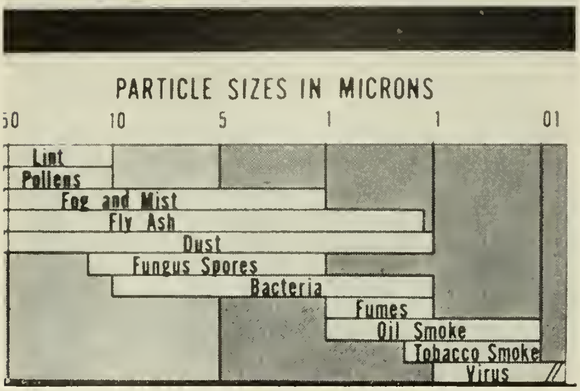

Fig. 1. Particle size in considering air cleaning devices

5) is composed of a series of glass or cellulose fibers or metal plates to which high voltage is applied. This establishes an electrostatic field and attracts airborne particles. The filter has an efficiency of 30 to 50%. It also has some serious disadvantages, one of which is that the charged media filter is also affected by humidity. As the humidity rises, the efficiency decreases. Many of these filters must also be replaced periodically which adds considerably to the cost of maintenance.

One of the best ways to remove airborne particles is by an electronic air cleaner. A high-voltage direct current is fed into an electrode in the center of a metal cylinder. Smoke and fumes receive an electrical charge and are attracted to the metal cylinder. This type of device developed by Cottrell in 1905 (Fig. 6) is used today for removing smoke and soot from industrial plants.

The two-stage, electrostatic precipitator was developed during the 1930s by G. W. Penny. Figure 7 illustrates how the two-stage system functions. Note how the high-voltage, DC current is fed into the first stage, the ionizing chamber. In this chamber, the airborne particles are given a strong electrical charge. The charged particles are then carried into the second, or collecting, section. Here, another strong electrical field is set up between a series of metal plates charged positively and negatively. Most of the particles coming from this ionizing section carry a positive charge. In the collection section, the particles are attracted to the negative plates. Conversely, the particles carrying a negative charge are attracted to a positive plate.

Electrostatic precipitators can stop more than 90% of the microscopic solids afloat in the air, including bits as small as 0.001 μ (Fig. 8). Some air cleaners also advertise that their units aid in

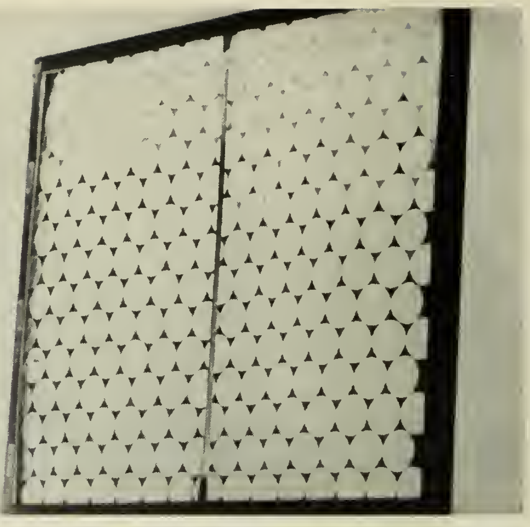

Fig. 2. A common filter—the viscous impingement form

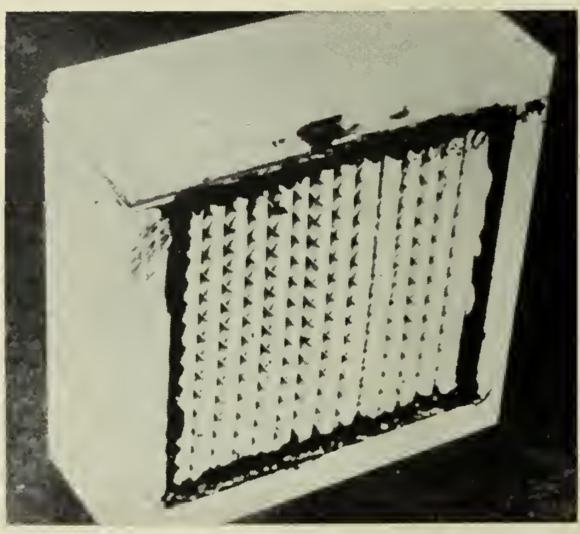

Fig. 3. The dry type of roughening filter

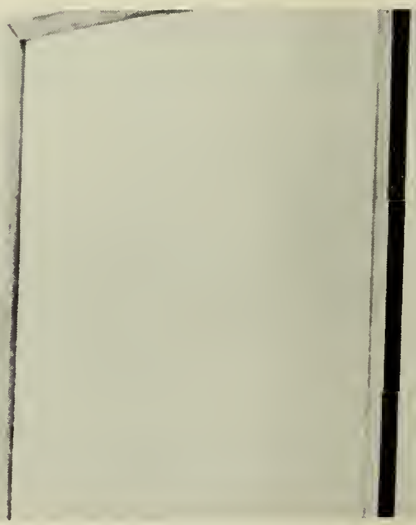

Fig. 4. The self-charging electrostatic filter

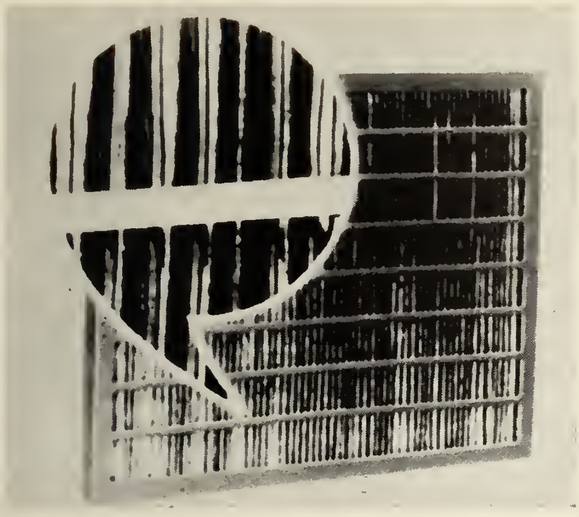

Fig. 5. The charged medium electrostatic filter

air ionization, although a good two-stage electronic air cleaner does not alter the normal concentration significantly. Some positive and negative ions are always present in the air. Usually, there is a slight preponderance of positive ions over negative ions. In the past few years, many reports have appeared which suggest that a high concentration of negative ions may be helpful in relieving many conditions such as hay fever, asthma, migraine, and so on, and a negative ion concentration in excess is believed to increase work efficiency. Positive ions are assumed to have the opposite effect. There may be some scientific basis for the above statements, but there are many overstated claims made for ionizers, and, therefore, caution concerning their use should be taken.

The Aerospace Medical Division of Wright-Patterson Air Field Base in Ohio examined the effects of ionized air on human behavior and concluded that there was no statistically significant difference in behavior of the type studied when using an excess of either negative or positive ions in concentration. In May of 1962, a second investigation determining the effects of ionized air on decision making and vigilance performance was evaluated, and, again, the conclusions were that there were no definite effects of ions on performance of the tests studied in that experiment.

AIR FILTER EVALUATION PROCEDURES

Confusion has existed due to the various methods of evaluating filter performances. Efficiency studies on particle removal are divided into three general methods. [1] The weight method in which a quantity of material is fed into a filter and its efficiency is obtained by measuring the retained portion. [2] The Dust Spot Staining Method in which samples of air are drawn through white filter papers of high efficiency before and after the cleaner. These sample papers are then evaluated with a photometer to measure the light-blocking property of the resulting stains. The efficiency is then calculated by comparing this staining power of the air samples upstream and downstream. [3] The third method is the particle count method in which samples of air are drawn upstream and downstream of the device being tested. The efficiency is calculated by counting the particles in the same air volumn entering and leaving the device. A throwaway glass panel filter, the type commonly used in residential systems, will have a weight efficiency of about 50 to 80%. On a stain basis, it will be about 5 to 8% efficient; however, on a particle count basis it will be less than 1%. On the other hand, if one were interested in ragweed pollen alone, which is very uniform in size, and no other contaminant were present, all three methods would yield approximately the same value. Roughing filters are commonly evaluated by the Air Filter Institute weight test where artificial dust, much coarser than atmospheric dust, is fed. There are no standards on the minimum efficiencies so obtained, however. This test practically ignores particles below 5 μ.

There is also no agreed standard for evaluating pollen or virus efficiency of a filter. In the evaluation of high performance filters, there are two basic standards for testing. The first is the National Bureau of Standards' dust-spot method, and, recently, the Air Filter Institute dust-spot method is being certified. The Air Filter Institute is composed of about twenty members who are creating policies and standards which will be helpful in evaluating filters.

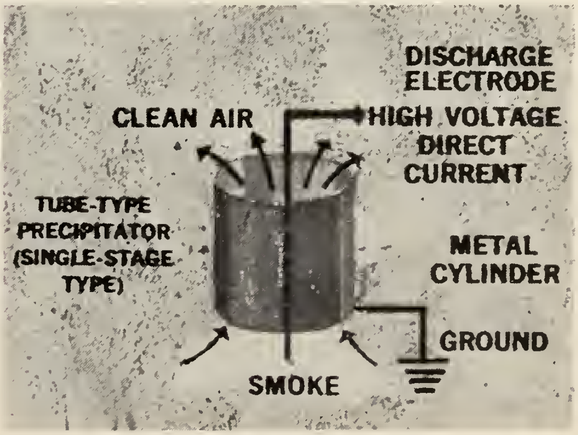
DISCHARGE ELECTRODE
CLEAN AIR
HIGH VOLTAGE DIRECT CURRENT
TUBE-TYPE PRECIPITATOR (SINGLE-STAGE TYPE)
METAL CYLINDER
GROUND
SMOKE

Fig. 6. The electric air cleaner

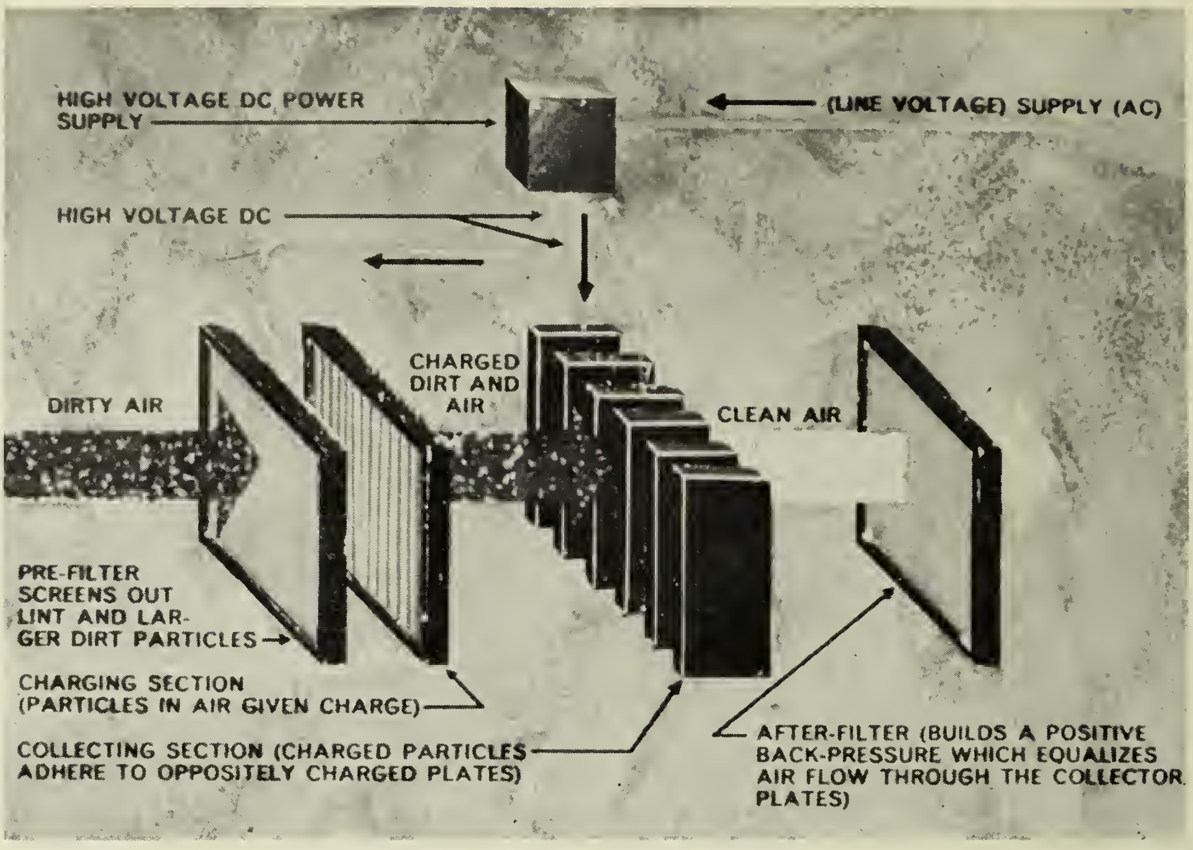
HIGH VOLTAGE DC POWER SUPPLY
(LINE VOLTAGE) SUPPLY (AC)
HIGH VOLTAGE DC
CHARGED DIRT AND AIR
DIRTY AIR
CLEAN AIR
PRE-FILTER SCREENS OUT LINT AND LARGER DIRT PARTICLES
CHARGING SECTION (PARTICLES IN AIR GIVEN CHARGE)
COLLECTING SECTION (CHARGED PARTICLES ADHERE TO OPPOSITELY CHARGED PLATES)
AFTER-FILTER (BUILDS A POSITIVE BACK-PRESSURE WHICH EQUALIZES AIR FLOW THROUGH THE COLLECTOR PLATES)

Fig. 7. The two-stage, electrostatic precipitator

AIR FILTER PERFORMANCE

Since every filter has a function of cleaning air as its prime purpose, it is of interest to understand its capabilities in terms of removing certain particle sizes. Electronic air cleaners perform very well to a fractional micron range. Cigarette smoke which falls between 0.001 and 1 μ may easily be removed by an electronic air cleaner. Bacteria, mold, and fungus, which are in the 1- to 5-μ range, are also effectively removed.

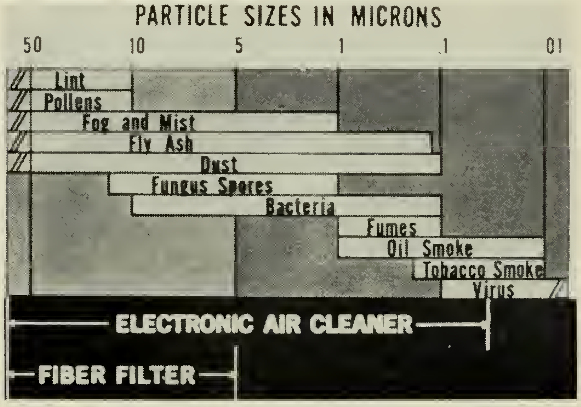

Fig. 8. The efficiency of electronic air cleaner over fiber cleaner

Pollens range in size from 10 to 100-plus microns in size, and most two-stage electronic air cleaners have efficiency of 99-plus percent on ragweed pollen. A 2-in. filter glass impingement type filter has a pollen efficiency of approximately 75%. Permanent impingement filters have pollen efficiencies of approximately 25 to 35%, and this is increased to 70 to 75% with the addition of an adhesive. The conventional 1-in. fiber glass filter has pollen efficiencies of approximately 55%. Mechanical filters of the viscous impingement type may be as high as 80% efficient for particle sizes about 10 μ. They are virtually ineffective for particle sizes of 5 μ or below. Virus ranging in size from less than 0.001 of a micron through 1 μ are capable of being removed from the airstream, but they are very difficult to identify on a count.

The fact that a filter is 98 to 99% effective in removing pollen is only one part of the story. This may be true in a wind tunnel when a given amount of pollen is released at one end and measured by the pollen count. What actually happens in a room may be a different problem. It is estimated that in a normal room with windows and doors closed there will be a complete change of air in one hour due to the leakage of air. This will vary with the amount of outside air and the wind velocity. An effective air cleaning device for an average bedroom should have a flow rate of at least 100 cu. ft. per minute with a high-efficiency filter or at least 200 to 300 cu. ft. per minute with a low-efficiency filter if the pollen is the important contaminant. Most low-priced units cannot move enough air to deem them beneficial. The usual room air conditioners have capacities of 150 to 400 cu. ft. per minute with very low-efficiency filters. A room 12 by 15 ft. with an 8-ft. ceiling has 1,440 cu. ft. of air. In addition, new air enters constantly and carries with it new contaminants. In a well-constructed house, this infiltration will result in a complete changeover in the air in about one to two hours. With new air flowing in constantly, no air cleaner will ever eliminate all the air contaminants present. Under the best circumstances, it can only reduce the level of contamination. At some point, an equilibrium will be reached, and no further reduction in the contamination level will take place no matter how long the air cleaner operates.

CONCLUSION

An urgent need for a standardization of air cleaning devices is present. There is a fairly good way to evaluate the ultra, high-efficiency filters and electrostatic precipitators. There are no practical standards used at the present time for the roughing filters. The weight method which is commonly used to evaluate roughing filters is of little value. There is no agreed standard for the evaluation of pollen or virus efficiencies.

The Air Filter Institute is attempting to create even more policies and standards which will be helpful in evaluating filters and does deserve our support.

THE MOST COMMON CAUSE of unilateral renal atrophy is ischemia, not chronic pyelonephritis. However, microscopic examination of most atrophic kidneys supplied by nonobstructed renal arteries reveals evidence of chronic pyelonephritis. Patients with ischemic renal atrophy have more severe hypertension, are older, and have poorer results frcm nephrectomy than those having pyelonephritis. About one-third of patients having renal atrophy with secondary arterial disease also have demonstrable occlusive disease in the opposite renal artery, and arteriography is therefore mandatory before nephrectomy. Every hypertensive patient with a unilateral atrophic kidney should have an angiogram. Characteristically, arteriosclerotic occlusive lesions occur at the renal artery orifice and can be easily missed by the pathologist. When stenotic lesions in the contralateral renal artery threaten renal function, restoring normal circulation of the opposite kidney should take precedence over removal of the atrophic kidney. When revascularization is satisfactory, the atrophic kidney can be excised at the same operation unless it can be revascularized or seems to be contributing significantly to total renal function. Renal angiography was performed on 75 hypertensive patients having unilateral renal atrophy. Results showed that 53 of these patients had enough occlusive disease in the artery supplying the atrophic kidney to explain atrophy by ischemia.

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Spread of Pulmonary Coccidioidomycosis Associated with Steroid Therapy

Report of a Case with a Lupus-Like Reaction to Antituberculosis Chemotherapy

MAJOR FREDERICK L. JONES, JR., MC, USAF, and
LIEUTENANT COLONEL CHARLES G. SPIVEY, JR., MC, USAF

Belleville, Illinois

INTRODUCTION

The availability today of a variety of potent therapeutic agents adds emphasis to the need for precise diagnosis in patients with pulmonary diseases. Knowledge of the underlying pathological process makes rational therapy possible by permitting both the selection of appropriate treatment and the avoidance of therapeutic measures which are contraindicated in the presence of a particular disease.

A case is presented wherein the patient, while receiving para-aminosalicylic acid (PAS) and isoniazid (INH) for presumed pulmonary tuberculosis, developed drug-induced systemic lupus erythematosus. When adrenal corticosteroid therapy was used in the management of this iatrogenic complication, marked exacerbation of previously undiagnosed pulmonary coccidioidomycosis occurred.

CASE REPORT

A 53-year-old Caucasian man was admitted on Sept. 5, 1962, to USAF Hospital, Scott Air Force Base, for evaluation of bilateral upper lobe pulmonary disease. Numerous chest films from 1951 to 1958 had reportedly revealed no significant abnormalities. In early 1959, while living in Arizona, he had pleuritic chest pain for a week. A chest film taken in late 1959, which was available for review, was negative except for minimal fibrotic markings at the extreme left apex. In May 1962 he noted productive cough, fatigue, and malaise. A chest film demonstrated bilateral upper lobe infiltration and fibrosis. Extensive studies in July 1962, including bronchoscopy, scalene node biopsy, sputum cultures for acid-fast bacilli and fungi, and 3 LE-cell preparations, were all negative. Shortly thereafter he developed pain, swelling, and limitation of motion in the left shoulder which responded slowly to symptomatic measures and hydrocortisone injections. In July 1962 he developed bilateral sciatica which gradually disappeared. Because of persistent abnormalities noted on serial chest films, he was transferred to USAF Hospital Scott.

Past medical history included episodes of pneumonia in 1943, 1951, and 1954. During his twenty-one years of active military service he had spent tours of duty in the mid- and southwestern, north- and southeastern United States and in Iceland, England, Labrador, and the South Pacific. His work had not involved exposure to noxious fumes or dusts. He gave no past history of drug reactions or atopic symptoms.

The patient appeared well nourished but chronically ill. Positive physical findings were otherwise entirely limited to the chest where breath sounds were increased in intensity over both upper lungs.

Roentgenograms of the chest demonstrated a diffuse infiltrate in both upper lobes associated with considerable fibrosis and upward retraction (Figure 1). Body section films revealed multiple small cavitations in the left upper lobe. Roentgenograms of the hands and shoulders were normal. Forced vital capacity was 71% and maximum breathing capacity was 94% of predicted normal values. The one-second forced vital capacity was 94% of the observed total vital capacity. Complete blood count, urinalysis, serologic test for syphilis, liver and renal function tests, latex test for rheumatoid factor, total serum proteins, and electrophoresis gave results which were negative or within normal limits. Complement fixation tests for coccidioidomycosis, histoplasmosis, and blastomycosis showed no titers. Skin tests produced positive reactions to first strength purified protein derivative (1 tuberculin unit), 1 to 100 coccidioidin, and 1 to 100 histoplasmin. Sputum cultures grew only normal respiratory tract flora. Multiple sputum and gastric specimens were negative on both smear and culture for acid-fast bacilli and fungi.

FREDERICK L. JONES, JR., *is now with the Department of Internal Medicine, Geisinger Medical Center, Danville, Pennsylvania (address for reprints).* CHARLES G. SPIVEY, JR., *is with the Departments of Internal Medicine and Pulmonary Diseases, U.S. Air Force Hospital, Scott Air Force Base, Illinois.*

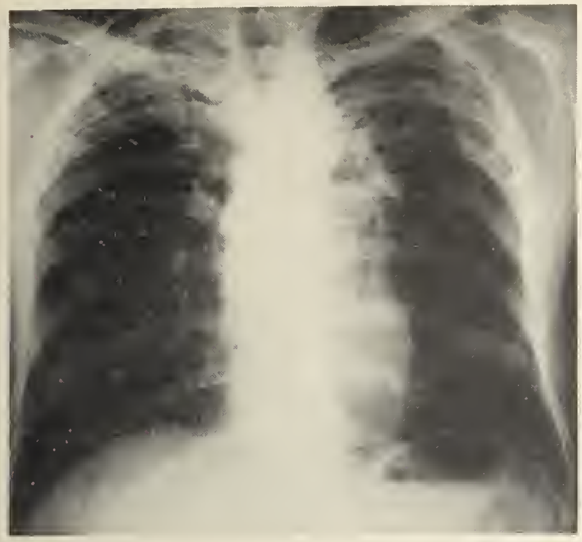

Fig. 1. Chest film of September 1962, showing infiltration and fibrosis in both upper lobes with upward retraction. No changes were noted on serial examinations through early January 1963.

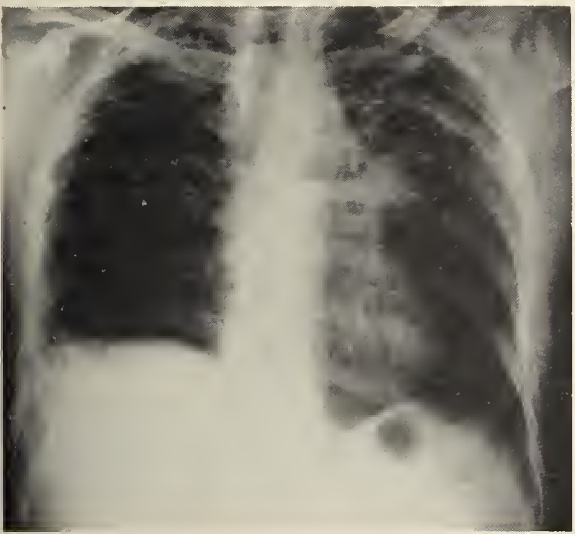

Fig. 2. Chest film of February 1963, demonstrating elevation of right diaphragm and small pleural effusion

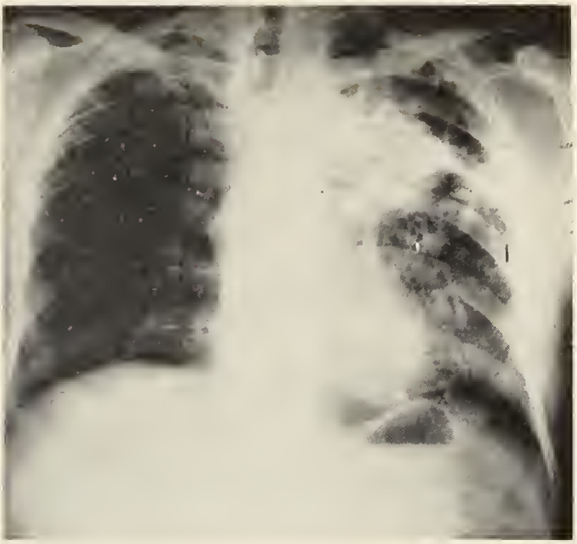

Fig. 3. Chest film of May 1963, demonstrating marked increase in pulmonary abnormality and large left upper lobe cavity. Multiple sputum cultures positive for *Coccidioides immitis.*

A tentative diagnosis for advanced pulmonary tuberculosis was made. On Sept. 15 therapy was begun with INH, 600 mg., and sodium-PAS, 15.5 gm. (equivalent to 12 gm. PAS), daily. Fifty milligrams of pyridoxine were given daily, and the patient also received occasional doses of dextropropoxyphene hydrochloride (Darvon®) and a preparation containing aspirin, phenacetin, and caffeine. He remained asymptomatic except for a mild cough and gained 6.4 kg. in weight. No fever, hepatomegaly, adenopathy, or rash were noted, and serial serum glutamic pyruvic transaminase determinations were normal over the first two months of chemotherapy. No changes were apparent on monthly chest films.

On Jan. 24, 1963, the patient complained of pleuritic chest pain, and a pleural friction rub was audible over the right lateral chest. A chest X-ray demonstrated a right pleural effusion (Figure 2). White blood cell count was 4,380 per cubic millimeter with a normal differential. The hematocrit was 43%. He remained afebrile with a normal pulse rate but complained of aching in multiple joints. Needle biopsies of the right lung and pleura obtained through the sixth intercostal space in the anterior axillary line on Feb. 1 revealed no abnormalities. A repeat needle biopsy of the left upper lobe on Feb. 20 showed nonspecific fibrosis of the lung and dense pleural scarring associated with evidence of chronic inflammation. No abnormality was demonstrable on needle biopsy of the liver. Pulmonary function tests showed a marked change since October 1962: vital capacity was 37% and maximum breathing capacity was 36% of predicted normal values; arterial oxygen saturation was 97.4% at rest but fell to 88.6% after fifteen minutes of exercise; arterial pCO_2 was 42.5 mm. of mercury and blood pH 7.42.

From Feb. 20 through 26, 5 consecutive LE-cell preparations were strongly positive. Although a drug-induced lupus-like phenomenon was considered, systemic lupus erythematosus was felt to be more likely in view of the history of joint complaints and the bilateral pulmonary disease of inapparent etiology. PAS and pyridoxine were discontinued on March 3. Administration of prednisone in a dosage of 80 mg. daily was begun on March 12, while INH, 300 mg. daily, was continued prophylactically. Pleuritic pain and articular symptoms improved progressively and disappeared entirely within two weeks. A repeat chest film revealed clearing of the right pleural effusion. Vital capacity doubled. Weekly LE-cell preparations remained positive through April 9 when only 1 typical cell could be demonstrated on 3 slides. Thereafter numerous preparations (18 in all) were negative through late October 1963.

In late April chest X-rays demonstrated marked deterioration of his pulmonary disease with soft infiltrates apparent bilaterally and large cavities in the left upper lobe (Figure 3). The patient began to produce copious amounts of sputum. The hematocrit had fallen to 31%. Cultures of 5 sputum specimens collected from April 24 to 30 were positive for *Coccidioides immitis.* Spinal fluid examination, including fungus culture, was negative.

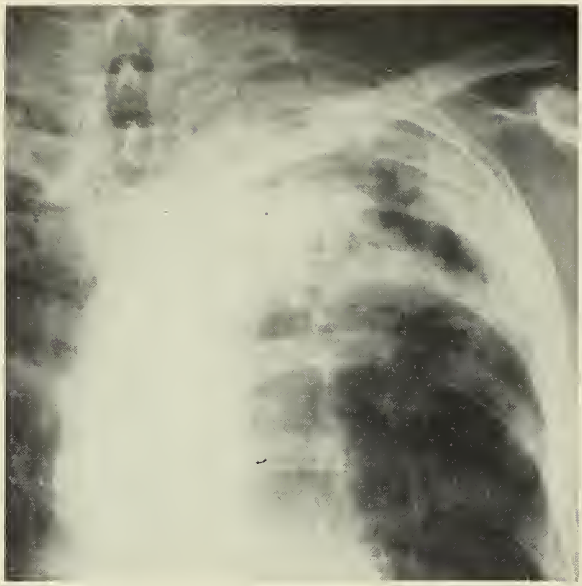

Fig. 4. Close-up view of left upper lobe in October 1963, showing nodular configuration of superior lining of cavity. This probably represents intracavitary mycetoma formation due to aspergillosis.

Steroid dosage was tapered and completely discontinued on May 29. Three units of whole blood were given, and therapy with intravenous amphotericin-B was begun. INH, 300 mg. daily, was continued.

Complement-fixation tests for coccidioidomycosis (which had been negative on Sept. 11, 1962; March 7, April 4 and 18, 1963), were positive on May 20 in a titer of 1 to 128 at Fitzsimons General Hospital. Sera tested in Dr. Charles Smith's laboratory gave a 4+ reaction at titers of 1 to 32 on May 20 and June 5. Amphotericin-B was administered until Oct. 30 in a total dose of approximately 4 gm. Fever, chills, anorexia, anemia, and moderate elevation of the blood urea nitrogen complicated his course. Weekly sputum cultures for *Coccidioides immitis* remained positive through Sept. 28 and were negative thereafter. From August through October, *Aspergillus* species was isolated from several sputum specimens. Multiple sputum cultures for acid-fast bacilli were consistently negative.

Serial chest films demonstrated minimal improvement bilaterally. The large left upper lobe cavity decreased in size, coincident, however, with the appearance of a nodular configuration of the cavity lining (Figure 4). Intracavitary mycetoma formation due to aspergillosis was thought to be highly probable.

Although 300 mg. of INH daily and occasional doses of Darvon®, aspirin, phenacetin, and caffeine were administered, weekly LE-cell preparations remained negative from April 19 through late October 1963. He was not rechallenged with PAS.

On Oct. 30, 1963, the patient retired from active military duty. Follow-up information through January 1965 has been kindly furnished by Dr. Robert D. Boynton of the Veterans Administration. No further amphotericin-B has been administered since October 1963. Serial chest films have revealed no progression, and the large left upper lobe cavitation has diminished in size (Figure 5). LE-cell preparations and tests for antinuclear antibodies have been negative through January 1965. Numerous sputum cultures for acid-fast bacilli and fungi have shown no growth. One complement-fixation test for coccidioidomycosis was positive with a titer of 1 to 8, but 2 others were negative. Despite exertional dyspnea, productive cough, and occasional slight hemoptysis, the patient has remained active and has gained 5.4 kg. in weight.

DISCUSSION

Although in the vast majority of cases of pulmonary coccidioidomycosis no further spread is noted after the original infection has subsided, a few instances have been reported of mild localized increase in the extent of previously quiescent, residual pulmonary lesions, sometimes with cavitation, months or years after the primary episode.[1] Recurrent infiltrative or cavitary disease is not infrequently noted following resection of coccidioidal pulmonary lesions. In the present case some bilateral increase in disease had occurred between 1959 and 1962, but the process had appeared quiescent radiographically for eleven months. The abrupt and severe local spread with cavitation which subsequently occurred was distinctly unusual and clearly associated with steroid therapy.

Since the introduction of adrenocorticotrophic hormone (ACTH) and the corticosteroids, there have been numerous reports of the appearance or spread of both bacterial and mycotic infections in patients receiving these agents.[2–4] Although steroids have been used successfully in erythema nodosum associated with coccidioidomycosis,[5] and at least 2 patients have recovered uneventfully from primary coccidioidomycosis acquired while receiving long-term steroids,[6] there is general agreement that such therapy is potentially hazardous.[7] Winn[8] lists administra-

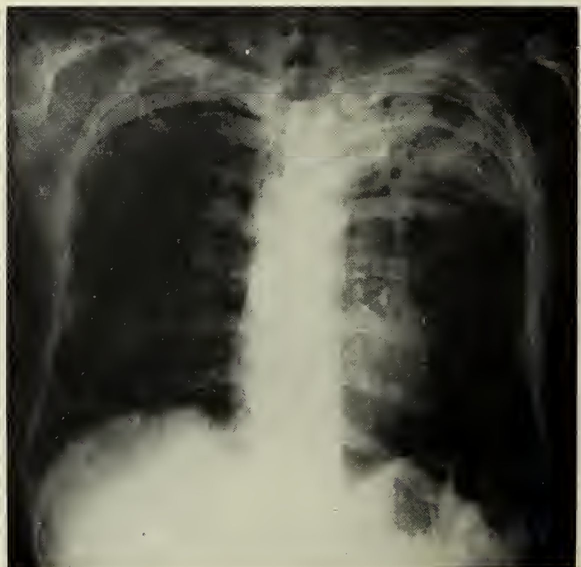

Fig. 5. Chest film of January 1965, showing slight improvement

tion of steroids as an indication for prophylactic treatment with amphotericin-B in patients with known coccidioidomycosis. Several investigators have noted that steroids have an adverse effect on the longevity of laboratory animals infected with *Coccidioides immitis* and other fungi.[9,10]

Despite such widespread uneasiness, there are only a handful of individual case reports documenting the spread of this mycosis associated with the administration of steroids. Castellot and associates[11] described miliary coccidioidomycosis found at autopsy in a patient with myelofibrosis who had received a prolonged course of prednisone. Bower,[12] Garb and Miller,[13] and DeNardo and associates[14] have described coccidioidomycosis associated with lymphomas, while Ellis[15] reported similar findings in a patient with sarcoidosis. Immunological mechanisms were abnormal in all cases reported. This was true in our case as well as where drug-induced lupus erythematosus and the immunosuppressive effects of steroid therapy coincided.

Certainly hundreds of patients living within the endemic zone with apparently healed or inactive coccidioidomycosis must have received steroids without complications. Nonetheless, the point is clear: steroids are capable of causing a disastrous local spread or wide dissemination of the fungus in individuals with stable, apparently inactive coccidioidomycosis, particularly in those patients with coexistent systemic disorders. To the well recognized danger of activation of tuberculosis by steroid therapy should be added an identical hazard in patients with the deep mycoses. This potential complication, for which convenient and satisfactory chemoprophylaxis is not available, should be seriously weighed when long-term steroid therapy is considered for any reason in patients with evidence of mycotic pulmonary infections, even if the process appears quiescent or healed.

Reactions to antituberculosis drugs are commonly encountered in clinical departments devoted to the care of tuberculous patients. The majority of these are due to PAS. Simpson and Walker[16] reviewed the literature concerning hypersensitivity to PAS and reported 45 additional cases in 1960. These authors noted no positive LE-cell preparations in their patients and cited only 1 reported case of such an occurrence. Review of the original case report,[17] however, fails to substantiate this. In 1961 Biekers and associates[18] described a man whose clinical course following therapy with both PAS and INH transiently resembled that of systemic lupus erythematosus with positive LE-cell preparations. Although they felt the reaction in their patient was probably due to PAS rather than INH, neither agent was subsequently administered in challenging doses. Zingale and associates[19] reported a case where such a reaction was clearly due to INH. Drug-induced lupus-like syndromes due to hydralazine,[20–22] anticonvulsant drugs,[23–25] and procaine amide[26,27] have also been recognized previously. Except for the fact that most of these are reversible, they are indistinguishable from idiopathic systemic lupus erythematosus clinically and pathologically. In most instances the responsible drug had been given for several weeks or months before a reaction occurred.[19,20,23] In contrast to idiopathic systemic lupus erythematosus, males are apparently affected as often as females.[20,21] High doses may precipitate the reaction, particularly in those instances related to hydralazine.[20,21]

PAS and INH had been given concurrently in customary doses for four months when our patient developed a lupus-like syndrome. Subsequent challenge with INH in therapeutic doses over the six months following recovery, however, failed to produce either symptoms or positive LE-cell preparations. Follow-up over a period of twenty-one months has failed to reveal any clinical or laboratory evidence of persistent or recurrent lupus erythematosus.

The possibility exists that our patient was desensitized to INH during the period when the drug was given "prophylactically" with steroid therapy. Patients who have reacted to antituberculosis drugs with various combinations of fever, rash, adenopathy, and jaundice may acquire a permanent tolerance to these agents when they are given in increasing doses concurrently with ACTH or adrenal corticosteroids.[28] Desensitization by this method in individuals with drug-induced lupus-like syndromes has, however, never been reported.

Our patient was not challenged with PAS since his severe steroid-aggravated coccidioidomycosis made avoidance of further steroid therapy imperative. It is a reasonable but not incontestable conclusion that PAS was the sole responsible agent in the production of this unusual reaction. No lupus-like reaction to PAS alone has been previously reported.

In the case presented, inability to establish a correct diagnosis resulted in the use of drugs (PAS and INH) to one or both of which a severe hypersensitivity reaction occurred. Corticosteroid therapy, given in the mistaken belief that idiopathic systemic lupus erythematosus was responsible for the entire clinical picture, resulted in progression of pulmonary coccidioidomycosis to a truly life-threatening degree.

Our purpose in presenting this case is threefold: [1] To demonstrate the potentially harmful effects of steroid therapy in patients with pulmonary coccidioidomycosis, [2] to report a lupus-like reaction to antituberculosis chemotherapy, most probably due to PAS, and [3] to emphasize the importance of establishing, where possible, the exact cause of pulmonary disease before employing potent therapeutic agents.

SUMMARY

A case is reported in which a lupus-like syndrome with positive LE-cell preparations developed during treatment with isoniazid (INH) and para-aminosalicylic acid (PAS) for presumed pulmonary tuberculosis. Withdrawal of PAS and institution of adrenal corticosteroid therapy caused complete disappearance of the lupus-like syndrome, but marked exacerbation of the patient's pulmonary disease, subsequently proved to be coccidioidomycosis, occurred. Prolonged challenge with INH produced no reaction, thereby providing evidence that PAS was probably the responsible drug. Follow-up has revealed no evidence of idiopathic systemic lupus erythematosus.

This case illustrates the hazards of steroid therapy in a patient with a stable, apparently quiescent pulmonary mycosis. The importance of establishing a precise diagnosis in patients with pulmonary disease before employing potent and potentially harmful therapeutic agents is emphasized.

The contents of this paper reflect the personal views of the authors and are not to be construed as a statement of official Air Force policy.

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The Patient with Spastic Paraplegia

GEORGE C. FLORA, M.D., and A. B. BAKER, M.D.

Minneapolis

SPASTIC PARAPLEGIA is generally caused by a spinal cord lesion below the cervical enlargement, implicating chiefly the thoracic cord and involving the long fiber tracts. Cases in which only the pyramidal tracts are involved show bilateral lower limb spasticity, manifested by slowing of gait and great difficulty in descending stairs. Many cases have both the pyramidal tracts and the posterior columns involved and show a subacute combined syndrome. The gait disturbance, then, depends on the degree to which each of these two long fiber tracts is involved, and, ultimately, the gait becomes spastic and ataxic.

Many intrinsic as well as extrinsic conditions may produce a spastic diplegia. For a large number of these conditions, there is specific therapy; thus an accurate diagnosis is very important.

The best guide to etiology for these conditions is the age of the patient, since different pathological processes are characteristic of different age groups.

INFANCY

Birth trauma (cerebral palsy). This disorder may not be apparent at birth or during the earliest months of life, when the baby does little more than eat and sleep. The diagnosis is usually suspected when the baby does not develop normal motor function and fails to kick, crawl, stand, or walk normally during the first twelve to eighteen months of life. Usually, this condition appears to be progressive during the early years of life and then becomes stationary or improves as the child develops compensatory mechanisms.

The signs of this neurological deficit are classic bilateral spasticity of the lower limbs, associated with hyperactive reflexes, clonus, and positive toe signs.

Therapy for this condition is twofold. Initially, serious deformities must be prevented from developing and, secondly, the child must be trained to utilize the remaining motor function to develop a walking pattern, first with physical assistance, then with aids such as Canadian crutches, and, finally, the child is taught independent walking. Spasticity is little benefited by present-day medications or surgical procedures.

Spinal cord tumors (generally metastatic). The development of spastic diplegia in this age range, either suddenly or rapidly progressive in an individual previously well, suggests an epidural granuloma, with cord compression or a vertebral body collapse from direct bony invasion and destruction. These conditions are frequently secondary to the reticuloses (Hodgkin's disease, lymphosarcoma, and reticulum-cell sarcoma). The early signs of this disease may be limited to bilateral pyramidal involvement or, if the process is more advanced, to a transverse myelitic syndrome, with loss of dorsal column, pyramidal tract, and spinothalamic function below the site of the lesion.

Treatment is directed toward immediate decompression if transverse myelitis has occurred. If the process is diagnosed before total compression occurs, X-ray therapy and chemotherapeutic agents are available.

YOUTH

Multiple sclerosis. This is one of the most common of all neurological diseases and is characterized by (a) onset between the ages of 17 and 35 years, (b) remissions and exacerbations, and (c) scattered central nervous system lesions. The spinal type of this disorder produces marked bilateral lower extremity spasticity which is frequently associated with ataxia due to disturbed posterior column function. In these cases,

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GEORGE C. FLORA *is assistant professor, Division of Neurology, University of Minnesota Hospital, Minneapolis, and* A. B. BAKER *is professor and director, Division of Neurology, University of Minnesota Medical School, Minneapolis.*

there may be genitourinary dysfunction relatively early in the course. Diagnosis can be established only if a history of remissions and exacerbations of multifocal lesions is obtained. Lesions frequently affect the visual-ocular, cerebellar, sensory, or vestibular systems, producing complaints of transient blindness or diplopia, incoordination, numbness, or dizziness.

Treatment of this condition consists of maintenance of good general health by establishing a regular pattern of rest, avoidance of exertion, and prompt attention to minor systemic infections plus a formalized long-term medicinal regimen. The medical regimen which is most beneficial at this time consists primarily of an oral therapeutic vitamin supplement; antihistamine, diphenhydramine hydrochloride (Benadryl®), 25 mg. three times a day; vitamin B_{12}, Lexavite, 1 cc. intramuscularly every two weeks; and adrenocorticotropic hormone, intravenously or intramuscularly, during acute exacerbations of the disorder.

Friedreich's ataxia. This condition is inherited, usually as a mendelian recessive, and tends to affect several brothers or sisters of an involved family. It generally begins between the ages of 5 and 10 years and is slowly progressive. The pyramidal tracts, dorsal columns, and spinocerebellar pathways are most frequently involved, producing a spastic ataxic gait. These patients frequently have associated skeletal deformities such as pes cavus and dorsal kyphoscoliosis.

Prognosis for a single case is unknown, as the disease may become arrested at any point in its progression, or it may progress to complete disablement. No specific therapy is available, but ambulation training and correct utilization of walking aids can be taught, and correction of deformities by surgical means is occasionally of benefit.

ADULT

Multiple sclerosis. This degenerative disease is the most common cause of spastic diplegia in the young adult. A careful history usually reveals previous transient neurological complaints such as vertigo, visual disturbances, paresthesia, and incoordination. As a rule, the neurological examination discloses evidence of the bilateral spastic paraplegia, as well as evidence of scattered involvement of the nervous system such as nystagmus, scotomata, decreased dorsal column function, internuclear ophthalmoplegia, decreased hearing acuity, or sensory deficits. The treatment of this disorder is discussed under the previous section.

Arsenic poisoning. This poisoning may occur in individuals employed in the manufacturing of chemicals and glass; in individuals who handle fruit sprays, sheep dip, and rodenticides; and in individuals who accidentally or intentionally are administered portions of this chemical. The spastic diplegia, which results from chronic poisoning, has an associated peripheral neuritis with severe burning paresthesias. The patient has severe gastroenteritic irritation from the chemical, manifested by anorexia, diarrhea, and colic. The diagnosis is suspected from rather frequent and classic dermatological manifestations of pigmentary changes in the axilla and dermatoses of the palmar and plantar surfaces of the hands and feet. The diagnosis can be established by laboratory means. Increased amounts of arsenic are recoverable from collected urine.

Treatment for this condition is dimercaprol, administered in a dosage range of 2 to 3 mg. per kilogram of body weight by intramuscular injections. The usual adult dose is a 2-cc. ampule containing 5% dimercaprol in oil; on the first day, 4 ampules should be given, on the second through the fourth days, 2 ampules a day, and 1 ampule daily on both the fifth and sixth days.

Lead poisoning. Lead intoxication occurs in employees of lead storage battery factories and in individuals who reclaim the lead from storage batteries by burning the casings in poorly ventilated buildings. Accidental lead poisoning from drinking water which is passed through old lead pipes or which comes from lead lined cisterns also is seen in rare instances. This intoxication produces a myelopathy with spastic diplegia and a peripheral neuritis, which classically affects the radial nerves, resulting in unilateral or bilateral wrist drop. The patient with lead intoxication will give a history of recurrent gastric colic during the period of greatest exposure. The classic "lead line" at the base of the gums and a pallor from anemia secondary to involvement of the hemopoietic system are often present. Laboratory tests show basophilic stippling of the red corpuscles, coproporphyrinuria, and increased excretion of lead (over 0.1 mg. percent) in the urine specimen.

Treatment for lead intoxication has been revolutionized by sodium calcium edetate (EDTA). This substance is given daily by slow intravenous injection, in doses up to 1 gm. per 15 kilograms of body weight, for four to five days. The regimen may be repeated after an interval if necessary.

Ergot poisoning. This substance is used extensively in the treatment of migraine headache in various forms such as ergotamine tartrate (Gynergen®) and ergotamine tartrate and caffeine (Cafergot®). Automedication with larger than recommended dosages and for long continued periods is not uncommon and produces a typical spastic diplegia and peripheral neuritis. The peripheral paresthesias are severe and in medical history are known as "St. Anthony's Fire." The peripheral involvement may be severe and result in gangrenous degeneration of the digits.

Treatment is discontinuance of exposure to the poison and relieving the discomfort. Bed rest and large doses of vitamins are used during the acute phase.

Beriberi. This condition occurs in chronic alcoholics and in patients who exist almost exclusively on an impoverished "polished white rice" diet, who have prolonged dietary restriction for weight reduction, and who follow certain food fads. The deficits most commonly seen are peripheral neuritis, spinal cord involvement with spastic diplegia, and posterior column deficit. Beriberi has a systemic deficit which involves the digestive tract, producing anorexia, nausea and vomiting, and severe abdominal distress. The myocardium is also affected, as manifested by tachycardia, cardiac dilatation, and, in some cases, by cardiac decompensation with dyspnea and edema.

Therapy of this condition produces dramatic remission of signs and symptoms. The most severe deficit is adequately treated with 30 to 50 mg. of thiamine hydrochloride administered intravenously in normal saline twice a day. Reversal of signs and symptoms is frequently noted within the first two days of treatment. Less severe deficits may be treated with oral thiamine hydrochloride in doses of 5 to 10 mg. daily. During the period of treatment, complete rest should be enforced to protect the impaired myocardial function.

Scurvy. This is a deficiency disease of vitamin C which may produce spinal cord involvement, manifested by a spastic diplegia. The condition has pathognomonic signs within the mouth if teeth are present and consists of bleeding gums and severe pyorrhea. The breath becomes extremely fetid. Hemorrhagic tendencies are common and may be observed in the mucous membranes of the nose and mouth, the subcutaneous tissues, the conjunctiva, and within the muscles or under the periosteum. The hemopoietic system is affected, with resultant severe anemias.

Treatment produces prompt remission of signs and symptoms and consists of administration of ascorbic acid, 1 gm. daily for a week, followed by 100 mg. daily for an indefinite period of time.

Primary pernicious anemia. This disease is the most common cause of subacute combined system degeneration in individuals over the age of 40 years. The gait disturbance which frequently results is associated with a peripheral neuritis. The neurological deficits may be preceded by, or be associated with, the macrocytic hyperchromic anemia from which the condition received its name. The condition is said to favor elderly, white-haired individuals who have long ears, and it characteristically gives a lemon-yellow color of the skin. The patients have a painful glossitis and an atrophic tongue. Laboratory tests will verify the type of anemia. An achlorhydria, even with histamine stimulation, and a positive Schilling test will confirm the diagnosis.

Treatment consists of intramuscular vitamin B_{12}, 1,000 μg. weekly, with crude liver extract, 2 units per cubic centimeter, 2 cc. intramuscularly weekly, until maximum improvement is noted, then supportive dosage of 1 injection of each per month for life.

Vitamin deficiency. Malabsorption secondary to surgical removal of the stomach or portions of the bowel, gastric carcinoma, obstruction of the bowel, or chronic diarrhea may simulate the neurological signs and symptoms of pernicious anemia. Frequently the blood picture is normal. This condition, once suspected, can be verified by a positive Schilling test.

The logical treatment is that of prevention. In any case, where surgical removal of the stomach or bowel has occurred, parenteral administration of vitamin B_{12}, 1,000 μg. intramuscularly, and of crude liver, 2 units intramuscularly, every month during the remaining lifetime of that patient, will protect that patient's nervous system. If the condition develops before the administration of these agents, then the regimen previously described for pernicious anemia should be followed.

Alcohol. This substance alone, or associated with dietary deficiencies (beriberi, pellagra, and scurvy), frequently causes myelitis in this age range. The myelitic involvement is primarily one of the lateral columns, producing classical pyramidal deficit which is associated with the more familiar "alcoholic neuritis." This neuritis produces a greater motor deficit than sensory disturbance except for marked hyperalgesia of the sole. The patient shows marked tremor of the extended fingers and tongue and usually has subtle or profound cerebellar disturbances.

Therapy is directed toward abstinence from the toxin, with liberal parenteral and oral vitamin supplements. The patient is best treated at bed rest and is given 1 gm. of ascorbic acid orally, 1 cc. of vitamin B complex (Betalin®), and 2 cc. of crude liver extract daily for fourteen days by intramuscular route. This regimen, plus adequate high-vitamin diet, frequently results in a marked improvement of neurological signs. This therapy may need to be repeated in obstinate cases.

Taboparesis. This classic offender cannot be excluded from a differential of spastic diplegia and ataxia developing in this age group. The findings of abnormality of the pupils (asymmetry, irregularity, or impaired response to light) will strongly suggest this diagnosis as a distinct possibility. Mental changes of any variety, suggesting organic psychosis or the functional psychotic states of mania, depression, or schizophrenia, when seen in an individual with myelitis of this type, strongly suggest this diagnosis. The absence of the Achilles reflex, when seen in a patient with posterior column deficit, and spastic diplegia, manifested by positive toe signs, are extremely suggestive of this condition. If pupillary abnormality, psychiatric disturbance, absent Achilles reflexes, and dorsolateral column signs are all found, the diagnosis is confirmed. Laboratory help is obtained if the serology is positive.

Treatment of one million units of penicillin intramuscularly for twenty consecutive days is therapeutically adequate if the neurological symptomatology improves. If neurological deficit continues to progress, then the treatment has been insufficient, and a repeated course, along with fever therapy, is indicated, regardless of serological results.

Cervical osteoarthritis. The transverse cervical bar that develops in this condition encroaches upon the spinal cord and produces bilateral pyramidal as well as dorsal column deficit of the lower extremities. This condition is slowly progressive and may suggest amyotrophic lateral sclerosis, especially if there are fasciculation and weakness of the hands. This condition may be diagnosed by cervical spine X-rays and myelography.

Treatment of this condition is surgical. Decompression at the site of cord damage is indicated and may serve to deter the progress of the disease, and, in some cases, it produces an improvement of symptomatology.

OLD AGE

Metastatic carcinoma of the spinal cord. The sudden appearance or rapidly progressive course of spastic diplegia with posterior column deficit in this age group always suggests the possibility of metastatic carcinoma. The presence of radicular pain or a history of weight loss in these patients should alert the physician to this possibility. The diagnosis is established by evidence of a primary lesion, any focal X-ray changes at the site of cord involvement, a cerebrospinal fluid block with increased protein on lumbar puncture, and an elevated sedimentation rate.

Therapy consists of immediate decompression and, later, the removal of the primary lesion. Deep X-ray therapy to the site of metastatic implant may be symptomatically helpful.

Vitamin deficiency. In the older age range, due to impoverishment or to poor eating habits, mixed patterns of vitamin deficiency are seen. The "starvation neuritis" shows myelitic signs, manifested by spastic ataxic gait disturbances. The signs and symptoms of beriberi, pellagra, and scurvy may be seen in part or in classic form. Therapy of this condition is useful. Parenteral supplement of the water-soluble vitamins initially, followed by continued oral administration of therapeutic vitamin supplements, as discussed in the previous section on alcohol, are recommended. The prognosis for return of the cord function is not good.

URINARY CATECHOLAMINES are elevated before vasovagal fainting. Epinephrine and norepinephrine thus may be important mediators of the first part of the diphasic response of vasovagal fainting and their increased secretion may be expressions of the physiology of anxiety. Catecholamines in urine samples collected before venipuncture in a group of students donating blood were higher in those who did, than in those who did not, subsequently faint.

JULIUS J. CHOSY, M.D., and DAVID T. GRAHAM, M.D., University of Wisconsin, Madison. Catecholamines in vasovagal fainting. J. psychosom. Res. 9:189-194, 1965.

Aged Cheese, Pargyline Hydrochloride, and Paradoxical Hypertension

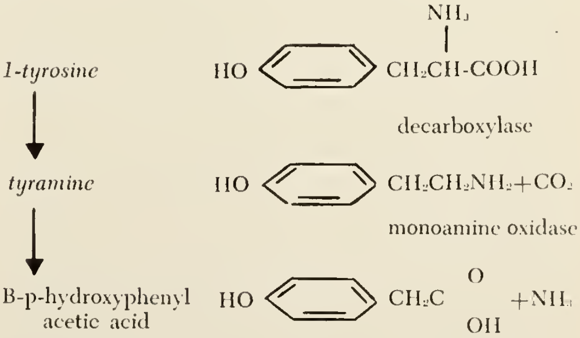
DAVID B. CARMICHAEL, M.D.
La Jolla

THE LAST TWO DECADES have seen the emergence of effective therapeutic measures directed against hypertension. Surgical techniques relating to renal arterial flow are currently achieving wide recognition, but the mainstay of treatment still is pharmacological. Antihypertensive agents differ widely in both mechanism and site of action. The clinician utilizing these compounds must be conversant with the alterations in body physiology created by drugs which affect vital enzyme systems, renal tubular function, autonomic nervous system, smooth muscle tone, or cardiac activity. Since derivatives of Rauwolfia serpentina and the initial thiazide compounds achieved widespread use, a host of new drugs have followed. Each drug has necessitated specific precautions. Rauwolfia derivatives have led to psychotic depression and gastrointestinal ulceration. Thiazide compounds may uncover latent gout, hyperglycemia, or result in profound hypokalemia if adequate precautions are not taken. Ganglionic blockade agents may precipitate severe cerebral vascular insufficiency. Hydralazine may mimic rheumatoid arthritis or disseminated lupus erythematosus, and bone marrow suppression has occurred. Anesthesiologists and surgeons have learned to anticipate occasional hypotensive reactions in the operating or recovery rooms in patients utilizing any of these medications. Even phenobarbital may result in fixed drug eruptions.

It is the purpose of this communication to emphasize one bizarre untoward manifestation of a monoamine oxidase inhibitor, pargyline hydrochloride (Eutonyl®).

In 1961 the monoamine oxidase inhibitors, which were being widely used in psychiatry and cardiology, were first reported to precipitate "paradoxical" sudden and severe hypertension.[1] A succession of clinical observations relating specifically to tranylcypromine (Parnate®) appeared, and in 1963 the relationship between the ingestion of cheese and hypertension in patients taking this drug was reported. Before this, potentiation of amphetamine (Biphetamine®), meperidine (Demerol®), and methylamphetamine by monoamine oxidase inhibitors had been described. In February 1964 the manufacturer of Parnate® temporarily removed this compound from the North American market, in view of the number of cases of transient hypertension occurring during its use, including the appearance of reports of associated serious intracranial bleeding.[2–21]

The biochemical rationale of the hypertensive effect of aged cheeses in patients receiving monoamine oxidase inhibitors appears logical and well understood. The normal sequence in the breakdown of tyrosine is noted below:



Intravenous tyramine has a powerful pressor effect. Under normal circumstances very little is absorbed through the intestine because it is destroyed by the abundance of monoamine oxidase in the bowel wall. Any absorbed tyramine not so degraded is transported to the liver where high concentrations of monoamine oxidase normally exist and the change to B-p-hydroxyphenyl acetic acid occurs. When monoamine oxidase inhibition is pharmacologically created, large amounts of tyramine may be absorbed into the

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DAVID B. CARMICHAEL *is with the Cardiovascular Service, Scripps Memorial Hospital, La Jolla.*

bloodstream unchanged, and marked and dangerous pressor effects result. Rarely, foods high in tyramine content may result in hypertensive effect in the absence of monoamine oxidase inhibition.

Aged cheeses are rich sources of tyramine. Asatoor reports Camembert to contain 0.2% tyramine.[22] New York State Cheddar has been reported to yield 1,416 μg. per gram of tyramine. Tyramine can be anticipated to be present in any circumstance where bacteria or molds have acted on protein for a prolonged period of time.

Eutonyl® is a new agent introduced for the control of hypertension. Among its actions is inhibition of monoamine oxidase. It is an effective drug in moderate and severe hypertension and has rapidly achieved wide use. In view of the problems experienced in the case of Parnate®, the manufacturers of Eutonyl® were quick to warn the medical profession when first reports of paradoxical hypertensive reactions appeared. A "drug warning" letter was forwarded to the medical profession in February 1964. Advertising literature and drug descriptions have clearly emphasized that the agent should not be used in conjunction with (1) Biphetamine® and its derivates (often found in appetite-suppressant preparations), (2) ephedrine (I-sedrine®) and nasal decongestants (often found in proprietary cold remedies), (3) aged cheese, (4) parenteral reserpine and guanethidine (Ismelin®), (5) imipramine (Tofranil®) and amitriptyline (Elavil®), (6) other monoamine oxidase inhibitors, and (7) methyldopa (Aldomet®). Phentolamine (Regitine®) parenterally is recommended for control of acute hypertensive reactions.[23] Agents such as chlorpromazine (Thorazine®) could also be anticipated to offer effective control.

Leonard, Gifford, and Williams have reported a patient with profound blood pressure elevation to 300+/180+ mm. Hg moments after ingestion of cheddar cheese while utilizing 50 mg. Eutonyl®.[24]

A similar case complicated by the appearance of severe anginal syndrome is described.

CASE REPORT

A 44-year-old salesman of Scotch ancestry was initially examined in cardiovascular consultation in March 1964. Hypertension had been present since 1957 and multiple medications had been utilized in an effort to obtain adequate hypotensive effects. Hypercholesterolemia was noted in 1962 and niacin, 0.5 gm., 3 times daily, was initiated. In 1962 anxiety symptoms were treated by meprobamate (Miltown®) taken during the day and diphenhydramine hydrochloride (Benadryl®), 100 μg., at night. D-alpha tocopherol (E-Ferol®) was also given in 1962. In mid-1963, because of inadequate blood pressure control by Rauwolfia derivatives and hydrochlorothiazide (Hydrodiuril®), and with pressures ranging from 190-220/130-150, Eutonyl® was initiated. A satisfactory fall in pressure to 160-180/95-100 ensued. Approximately one month after starting Eutonyl® the patient would periodically arise from bed complaining of crushing substernal distress radiating through to the back and down the left arm. There was associated breathlessness and occasionally heavy diaphoresis. The patient volunteered that this would occur when he would eat a late dinner in a restaurant. It had become a family joke that his wife always carried her "doggie bag" as they were seldom able to complete the meat course after a salad heavily laden with dressing. He reported that on several occasions he would necessitate "up to 2 dozen" nitroglycerin tablets to get through an evening after having ingested a Roquefort dressing. The family had also used Black Mountain Sharp Cheddar Cheese and he observed that "a few seconds" after swallowing a piece of this cheese intense, constricting chest pressure would appear. Over the passage of several months anginal syndrome began to occur with physical exertion. Pentaerythritol tetranitrate (Peritrate®) and Persantin® were started with some reduction in frequency of attacks of chest constriction. Aged cheeses would, however, consistently result in intense distress. On a single occasion where he could be examined following a meal containing Roquefort cheese, marked blood pressure elevation to 260/160 was recorded following an episode of chest pain and diaphoresis.

The past medical history was not remarkable apart from the hypertension. The patient's father died at 70 of an unknown cause. He had been hypertensive. His mother died at 68 as a result of chronic bronchial asthma. The patient smoked heavily and averaged 3 oz. of liquor daily.

Physical examination disclosed a tense, hyperactive Caucasian. Optic fundi demonstrated an arteriovenous ratio of one-half, with many A/V crossing phenomena and an increased arterial light reflex. The right carotid pulsation was reduced. No carotid thrill was palpable. A grade 2 systolic bruit was audible under the angle of the right mandible. A grade 4 systolic bruit was audible along the left carotid system. The right radial pulse was slightly reduced when compared to the left. Right arm blood pressure was 150/110, left arm blood pressure was 190/130, and right leg blood pressure was 210/140. The patient was in sinus rhythm. No precordial thrill was palpable. R2 exceeded L2. A low frequency grade 3 systolic murmur demonstrating midsystolic accentuation was widely audible. The murmur was maximal at the apex and was well heard at the base. No diastolic murmur was audible. Neck veins were not distended. Minimal varicosities were noted involving the left saphenofemoral system. He weighed 171 lb. The remainder of a comprehensive physical and neurological examination was normal.

LABORATORY PROCEDURES

Urinalysis was normal. Protein based iodine was 4.7, blood urea nitrogen was 14.5, fasting blood sugar was 104, uric acid was 7.4, and serum cholesterol was 244. The electrocardiogram and phonocardiogram are reproduced in Figures 1 and 2.

The patient was hospitalized and all medications except nitroglycerin and Peritrate® were discontinued.

A retrograde femoral arteriogram, utilizing the

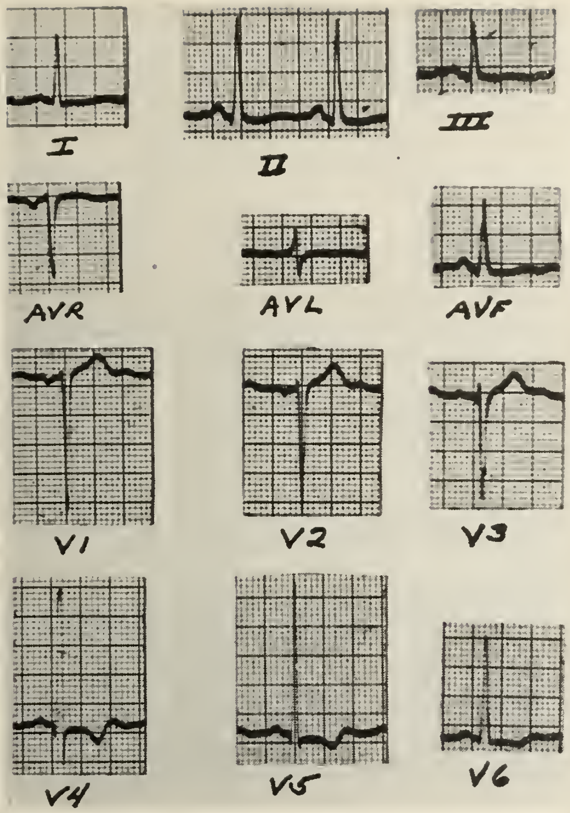


Fig. 1. Electrocardiographic tracings from patient with paradoxical hypertension associated with ingestion of cheese

Seldinger technique and including an arch aortogram and a renal arteriogram, was performed. Extensive atherosclerotic disease was demonstrated.

Bilateral renograms were performed utilizing radiohippuran. Decreased hippuran clearance, which was more marked on the left, was demonstrated.

Clearance studies under saddle block anesthesia were performed. Bilateral impairment in renal clearance was confirmed.

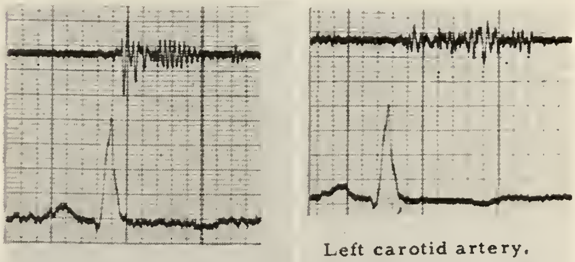
Lack of definitive evidence of unilateral impairment of renal circulation militated against a surgical attack on the apparent renal arterial lesion. The total lack of symptoms or signs of impaired central nervous system function, coupled with the extensive atherosclerotic disease, dictated medical treatment of his cerebral vascular disease.

The patient was placed on a low-calorie, low-lipid, low-sodium diet. He was given bishydroxycoumarin (Dicumarol®), with the prothrombin time being maintained at two times control. Nitroglycerin, Peritrate®, Miltown®, Hydrodiuril®, and Rauwolfia serpentina were prescribed. A program of progressive increase in physical activity with avoidance of heavy exertion has resulted in marked symptomatic benefit. Currently he averages 2 nitroglycerin tablets daily during a busy schedule and his blood pressure averages 145/85.

COMMENT

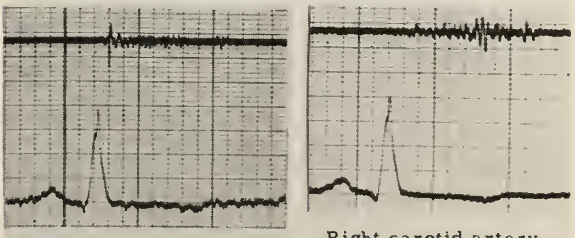
The universally nontoxic medication is yet to be dispensed. Public health and safety demand careful scrutiny of all pharmaceutical agents and with rare exception this is effectively carried out by the drug industry. When toxic or untoward manifestations of a new drug are reported it always becomes a difficult decision to balance the effectiveness of the drug in question against the potential harm that might ensue from its unwise administration. The frequency and severity of the reactions to Parnate® led to its temporary withdrawal from the American market. Reactions to Eutonyl® have been much less severe and, by careful adherence to the manufacturer's recommendations, seem totally avoidable.

The patient described in the preceding case report had evidence of advanced vascular disease. A relationship between cheese and paradoxical hypertension was apparent but not conclusive until information of this possibility was received from the manufacturer. Three weeks after discontinuance of Eutonyl® and with no other change in treatment, he was able to eat Roquefort cheese without difficulty. As other



Left sternal border, thin diaphragm, logarithmic microphone (5.0)

Left carotid artery, small bell, logarithmic microphone (5.8)



Apex, medium bell, logarithmic microphone (4.8)

Right carotid artery, small bell, logarithmic microphone (5.8)

Fig. 2. Phonocardiogram of patient taken on initial examination, March 1964

effective treatment has offered adequate control it was not considered necessary to return him to Eutonyl®.

SUMMARY

A case report emphasizes the necessity of recognizing the danger of concomitant administration of a monoamine oxidase inhibitor and foods high in tyramine content. Aged cheese and Eutonyl® resulted in marked hypertension and the appearance of disabling angina pectoris. As with all antihypertensive compounds, this drug must be prescribed only with full understanding of the side effects.

Appreciation is expressed to Anne L. Barlow, M.D., for her review of this manuscript.

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THE INCIDENCE OF TANGIER DISEASE—familial high-density lipoprotein (HDL) deficiency—is probably higher than suspected, and the disease occurs in adults as well as children. A good diagnostic indication is foam-cell infiltration of tonsil tissue. This manifests itself as an orange or yellow-gray coloring of the tonsils or mucosa after tonsillectomy or by a distinctive light-orange or yellow-gray ring surrounding the oropharynx. Other findings, regardless of age, include hypocholesterolemia without malabsorption, abnormal tonsils, and abnormal tissue storage of cholesterol esters, especially in corneas and the rectal mucosa in older subjects. There may also be unexplained enlargement of the liver, spleen, or lymph nodes. Concentrations of plasma cholesterol should be checked and if lower than 125 mg. per 100 ml., HDL concentrations should be determined. Paper electrophoresis is useful for HDL screening, but a positive diagnosis depends on immunochemical methods for identifying the lipoprotein. Reasons for HDL deficiency are unknown. Information is based on findings from two brothers ages 45 and 48, respectively, and from 4 children who had Tangier disease. One brother had hypersplenism and both had unusual infiltration of the corneas and rectal mucosa.

HARRY N. HOFFMAN II, M.D., and DONALD S. FREDRICKSON, M.D., Mayo Clinic and Foundation, Rochester, Minn., and National Heart Institute, Bethesda, Md. Tangier disease (familial high density lipoprotein deficiency). Amer. J. Med. 39:582-593, 1965.

Cytodiagnosis in Bronchial Carcinoma

HARVEY McTAGGART, M.B., Ch.B., M.C. Path.,
and MICHAEL WALTON, M.D., D.P.H.
West Hartlepool and Middlesbrough, England

THE FIRST published series of sputa examined for malignant cells was reported by von Hemplen in 1919; unfortunately, he used air-dried films, a technique which has since been regarded as unsatisfactory. With the introduction of wet-fixation,[1] good preservation of cell morphology became possible, and in a series of sputum examinations in suspected bronchial carcinoma, 68% of patients gave positive results.[2]

Since that time, while a small number of interested workers has kept the technique alive in this country,[3–7] the major development has taken place in the United States where progress in the whole field of exfoliative cytology was stimulated by the work of Papanicolaou and his school.[8] With the growth of a large body of experience, reliability has been much improved, particularly by the recognition of possible causes of false-positive results.[9–16] In recent years there has been a growing interest in the technique in Great Britain.

MATERIAL AND METHODS

The series reported here was obtained from patients referred to Poole Hospital, Middlesbrough, for investigation of chest symptoms. In each instance, bronchoscopy was carried out under a general anesthetic with thiopental sodium and succinylcholine chloride.

A consecutive series of 483 patients yielded 200 instances of proved bronchial carcinoma in a period of fourteen months from January 1, 1963. The diagnosis was confirmed by the histological examination of biopsy, surgical, or autopsy material in 123 of the patients with bronchial carcinoma. In a further 54, where no histological proof was available, the appearances at bronchoscopy were diagnostic, and in 23 patients in whom neither histology nor bronchoscopy supported the diagnosis the clinical course and radiological findings confirmed the diagnosis in each one.

The specimens examined were bronchial aspirates obtained at bronchoscopy and specimens of sputum obtained both before and after bronchoscopy. Bronchoscopic examination was carried out using a Negus bronchoscope. Specimens of the aspirate were obtained by bronchial suction and collected into 20 ml. of 50% ethyl alcohol (industrial methylated spirits) in a 250 ml. plastic bottle fitted with a special cap made by Oxygenaire, Ltd.[17] The bottle was inserted into the aspirator system just proximal to the end of the sucker, and normal saline was used to flush the more viscid material up the tube. The aspirate was collected during the whole of the procedure and the total specimen was kept for examination. On reaching the laboratory, the specimen was centrifuged and 2 smears were made from the deposit and fixed in 95% ethyl alcohol.

Specimens of sputum were collected into screw-capped tins, containing 20 ml. of 50% ethyl alcohol, when the patient first woke on the morning of bronchoscopy and on the 2 successive days where this was possible. Care was taken to ensure that both staff and patients were aware of the necessity of obtaining a good specimen.

In the laboratory, 2 smears were made from each specimen and fixed in 95% ethyl alcohol. All smears were first covered with a layer of celloidin and were stained by Papanicolaou's method with stains produced commercially by Ortho Pharmaceuticals, Ltd. The slides were carried in racks, which held 25 slides each, and were stained in staining dishes. After staining, smears were covered by a 1½ × ⅞ cover slip, and the whole of this area was examined. Malignant or atypical cell groups were localized for further reference by marking the cover slip with white ink.

Each specimen was reported as positive or negative. There was no intermediate category but in negative patients an additional report of "saliva only," "mostly saliva," or "atypical cells

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HARVEY MC TAGGART *is consultant pathologist, General Hospital, West Hartlepool, and* MICHAEL WALTON *is consultant chest physician, Poole Hospital, Middlesbrough.*

TABLE 1

CYTODIAGNOSIS IN RELATION TO BRONCHIAL BIOPSY

Total number of patients with bronchial carcinoma	200
Total number with positive cytology	169 (84%)
Total number with positive biopsy	83 (41%)
Total number with positive cytology and/or biopsy	176 (88%)

TABLE 2

DETECTION RATE IN RELATION TO NUMBER OF SPECIMENS EXAMINED

	Number of specimens examined per patient		
	1	*2*	*3*
Total number of cases examined	32	64	104
Number with positive cytology	21	54	94
Percentage detection rate	65	84	90

present" was sometimes made, and in the positive patients the cell type was reported.

RESULTS

As will be seen in Table 1, of the 200 patients with bronchial carcinoma, 169 were found to have a positive cytology in one or more specimens giving an overall percentage positive rate of 84; 31 cases (16%) were missed and of these, 6 had a positive biopsy. Bronchial biopsy was positive in 83 of the total number of patients which gave an overall percentage rate for biopsy of 41. When cytology and bronchial biopsy results are taken together, a total detection rate of 88% was obtained.

No false-positive results were recorded in this series. Atypical cells were reported on 15 occasions when no further positive specimens were obtained from the patient. In 10 of these it was subsequently shown that bronchial carcinoma was present and in 5 that the atypical appearances were due to nonmalignant changes in bronchial epithelial cells. These results show the importance of the examination of further specimens when atypical cells are seen.

The single specimen of total bronchial aspirate was positive in 132 patients (61%). This result is slightly better than that obtained by examining a single specimen of sputum, but the difference is not sufficiently large to warrant separation of the 2 results, so that for the purpose of this study they have been combined.

Table 2 shows that the number of positive results increases with the number of specimens examined in each patient. From the practical point of view, the optimum number of specimens examined appears to be 3 and should consist of a bronchial aspirate and 2 sputum specimens, as above this number the increase in accuracy of diagnosis is not commensurate with the increase in work load. Examination of 4 specimens did not increase the detection rate significantly.

DISCUSSION

Satisfactory results can only be obtained in the cytological diagnosis of bronchial carcinoma by careful attention to detail at every stage of collection and examination of specimens.

The collection of sputum specimens requires careful instruction both orally and in writing to the patient, so that he fully realizes what is required of him. The nursing staff too requires careful instruction and regular reminders.

By these methods it is possible to obtain a large number of satisfactory specimens, but there remains what we consider an irreducible minimum of unsatisfactory specimens mainly due to failure of the patient to produce deep cough sputum even after proper instruction. We have not yet had the opportunity to try the aerosol method of sputum production introduced by Bickerman, Sproul, and Barach,[18] which, it is claimed, would probably further reduce the failure rate.

Bronchial aspiration, bronchial washing, and bronchial swabbing are the 3 methods which have been used by various workers to collect specimens for cytological examination at bronchoscopy. We have chosen bronchial aspiration since it has proved the most satisfactory.

The method used was that already described when all the material aspirated during the bronchoscopy was collected for examination, including bloodstained material aspirated following biopsy. Before adopting our present technique, other methods which collected only part of the aspirate were found to be less successful.

The choice of specimens for examination was to a certain extent dictated by circumstances, as many of the patients in the series were admitted from elsewhere for only a few days in order to have a bronchoscopic examination. It was decided, therefore, to examine in as many patients as possible the sputum obtained before bronchoscopy, 1 or 2 specimens obtained on the days immediately afterward, and the bronchial aspirate obtained at bronchoscopy.

It is widely held that postbronchoscopic sputa are a source of confusion and may lead to false-positive results.[19–21] In this series we have examined 430 sputa obtained after bronchoscopy; this has never been the cause of error and, indeed, in 6 cases the postbronchoscopic specimens gave the first correct positive results. We therefore consider the examination of postbronchoscopic specimens of sputum as most valuable.

A number of different staining methods have been used in the preparation of smears for cytological examination—some with excellent results—but we would not support Hinson and Kuper in their assertion that no particular staining technique has any special merit.[20] Using unfixed wet preparations stained with methylene blue, their total detection rate was 60% and rose to only 71% after the examination of 5 specimens. They also admit to missing 64% of all oat cell carcinomas with this method.

Andrews and Rosser[21] using a cell block technique stained with hematomylin and eosin concluded that exfoliative cytology failed as a simple screening test because results were so poor.

While not asserting that all other staining methods are inferior to Papanicolaou's method, we have found it clear, accurate, and productive of slides capable of being stored for future reference. Since it is the stain most widely and successfully used in cervical cytology, it would seem reasonable to advocate its use in the other branches of exfoliative cytology as well.

An overall detection rate of 80% or more has been obtained by Wandall (84%),[22] Clerf and Herbut (88.8%),[23] Sirtori (92.5%),[24] and Koss and Durfee (80%),[14] but it was generally accepted that only satisfactory specimens should be included in the analysis. In our series with an overall detection rate of 84% and a detection rate of 90% where 3 specimens were examined, we have not excluded the unsatisfactory specimens even when these consisted only of saliva, since a certain number of poor specimens are inevitable in any series. The inclusion of these specimens therefore gives an accurate indication of the value of the method in clinical work.

Andrews and Rosser[21] state that, "It seems likely that with the more readily available thoracic services and the decreasing surgical risk, exploratory thoracotomy will be used more frequently and provide a more realistic approach to the early diagnosis of lung cancer."

We would strongly oppose this view on the grounds that exploratory thoracotomy carries a definite morbidity and mortality rate and that, on as many occasions as is possible, histological or cytological proof for the diagnosis should be obtained before surgical intervention.

The detection rate for biopsy histology in our series is 41% which, although low, is higher than some other reported series (Duguid and Huish,[25] 31.2%, and Hinson and Kuper,[20] 31%).

With a total detection rate of 84% for cytology, twice that of biopsy alone, there can be no reasonable doubt that cytology is a valuable diagnostic aid in bronchial carcinoma.

There has been an increasing interest shown in exfoliative cytology in this country in recent years, culminating in the formation of the British Society for Clinical Cytology and in the establishment throughout the country of centers of cytological diagnosis. Although most emphasis has been placed on gynecologic cytology, we feel that a useful field for screening tests would be found in sputum examination of patients in the cancer age groups reporting to their general practitioners with respiratory symptoms. Vernon Thompson,[26] when recommending independent access for general practitioners to X-ray departments, stated that, "The delay in diagnosis of carcinoma of the lung is not due to the failure of patients to report their symptoms to their doctors. It is largely due to the failure of the medical profession as a whole to diagnose carcinoma of the lung at an early stage."

The analysis of 135 cases of patients submitted to operation at the London hospital in 1954 showed an average delay of 6.4 months between the first symptoms and attendance at the department of thoracic surgery, of which only 1.5 months on the average was due to delay by the patient in seeking medical advice.

More widespread use of sputum cytology by general practitioners and chest physicians could reduce the delay in many instances, as the patient would be referred at once to the thoracic surgeon.

SUMMARY

A consecutive series of 483 patients admitted for chest investigation yielded 200 instances of bronchial carcinoma. Eighty-four percent were positive on cytological examination of bronchial aspirate and sputum.

The importance of care at all stages of the cytological investigation is stressed and a suggestion made for more widespread use of the methods described for the earlier diagnosis of this increasingly common disease.

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LEAKAGE AT THE SUTURE LINE may increase postoperative mortality in epiphrenic diverticulectomy if associated defects of the diaphragm and lower esophagus are not simultaneously corrected. Most common defects are hiatus hernia, diffuse spasm, and achalasia. The severity of symptoms, size of the diverticulum, and the presence of associated defects determine candidates for surgery. Epiphrenic pulsion diverticula is asymptomatic and requires no operation in about one-third of the cases and medical management often is possible for long periods in poor-risk patients with mild symptoms.

THOMAS H. ALLEN, M.D., and O. THERON CLAGETT, M.D., Mayo Clinic and Foundation, Rochester, Minn. Changing concepts in the surgical treatment of pulsion diverticula of the lower esophagus. J. thorac. cardiovasc. Surg. 50:455-462, 1965.

ACID-CITRATE-DEXTROSE (ACD) blood is preferable for primary filling of the pump-oxygenator in cardiopulmonary bypass. Before perfusion, blood is collected into ACD solution, diluted, and treated with additives. Platelets may be separated optionally before placement of blood in the pump-oxygenator and then administered after bypass termination. Hemodilution techniques improve urinary flow rate during and for several hours after bypass as compared to those using whole blood. ACD blood may be used for all patients with all types of lesions. Special blood bank materials and techniques are not needed and since any unused blood has a twenty-one-day shelf life, it may be returned to the blood bank. Whole heparinized blood was used in 2,075 perfusions, diluted heparinized blood in 1,350, and diluted ACD blood in 600. There were no significant differences in coagulation factors, renal performance, acid-base profile, electrolyte levels, serum albumin concentration, hematocrit value, or clinical findings in patients receiving diluted heparinized blood and those receiving ACD blood.

ALAN D. SESSLER, M.D., HOWARD F. TASWELL, M.D., EMERSON A. MOFFITT, M.D., and JOHN W. KIRKLIN, M.D., Mayo Clinic, Rochester, Minn. Heparinized versus acid-citrate-dextrose blood for cardiopulmonary bypass Mayo Clin. Proc. 40:859-867, 1965.

RUTH E. BOYNTON *Series*

School Health—Its Problems and Challenges

MILDRED E. DOSTER, M.D.

Denver

IT HAS BEEN SAID that the most constant thing in the world is change. Efficient health work in our schools must reflect, therefore, the significant changes in old conditions and developments in new ones as they affect today's children and youth.

Dr. Ruth Boynton realized this throughout her many years of fine service in Minnesota and was aware that school and college health work must either adapt or retrogress. In this special article I shall try to outline 6 of the most most obvious current problems in school health. Being alerted to them, hopefully, will stimulate constructive thinking to meet and solve them most adequately for our times.

1. *Increasing numbers of the school age population.* According to *Changing Times,* The Kiplinger Magazine, February 1965, elementary and secondary enrollments will jump from the present 36 million to 44 million by 1970. This will require half a million new classrooms and we are now building about 70,000 a year. Not only are more children in school each year, but our schools now hold higher proportions for longer times. Twenty years ago, half the 17-year-olds graduated from high school; now 70% do. Teacher training is better and more men are entering the profession. Now, a majority of high school teachers are men. Last year we spent an all-time high of 35 billion dollars for education, 150% more than a decade ago, and about 70% of this was for the nation's regular elementary and secondary schools. Dr. Conant in 1958 urged that we spend 7 or 8 billion more to meet the educational deficit that has been developing in this country when schools and staffs have failed to keep up with the increasing population and to utilize a more fair share of the tremendous growth in our national economy. The average annual expenditure per child is $155 for education and a few extra dollars for both school and community health. Many are unable or unwilling to comprehend this rapid quantitative change in our population. But swelling numbers of pupils continue to overflow buildings and facilities and require expanded services. With 44 million school age children to be served by many various health procedures, some shortcuts and curtailments must be considered.

2. *Shortage of health personnel and community resources to carry on routines previously recommended.* One change that is steadily spreading over the country is the policy of doing less frequent routine health screenings and medical appraisals. Although there are an estimated 11,000 full-time school nurses; several thousand public health nurses giving part-time to schools; a few thousand dental hygienists, audiologists, and health educators; and several hundred physicians in schools part-time and full-time, the ranks are still too thin to carry out extensive programs in most of the nation. Again, newer ways must be developed to have the few professional people serve the most pupils to their best advantage.

3. *More research and further application of new knowledge in school health procedures and methods.* There are many practical problems as to how examining physicians, nurses, audiologists, dentists, dental hygienists, psychiatrists, and all types of educational personnel can best function in the school health program. Also, more attention has been given recently to the role of volunteers or those nonpay assistants from outside the schools. The worth of many of the earlier routing procedures is being challenged—often with little accurate or valid evidence. Much more careful accumulation and analysis of data must be done, lest schools make changes just to discard the old and adopt new suggestions. Considerable re-

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MILDRED E. DOSTER *is assistant director, Health Services, Denver Public Schools.*

search is occurring on growth, nutrition, exercise, reading skills, brain damage conditions, and disease controls. To apply what is known is as important as seeking additional answers to our many unsolved problems in school health.

Routine audiometric and vision screening services are other areas that should receive more critical study. How often should these be done, on what types of pupils, by whom, and what benefits accrue to the pupils? Typical of this need to question programs and discard the relatively useless and outmoded procedures is an analysis reported from the Denver Public Schools on 994 graduating seniors who had experienced repeated testing throughout their school years. It revealed that 85% of all those who developed significant hearing losses had done so by the end of the third grade. Thus, it seems audiometry should be concentrated on the lower elementary age children with less frequent screening in older years. Growth checks, tuberculin tests, and vision screening, likewise, may be done too often to be worth the time of scarce personnel or in school interruptions and benefits to the pupils. While routines can be done too often, far more children in the nation receive too little attention, and the latter condition tends to be continued as long as the younger population groups need more services than can be rendered by trained personnel from a less numerous population group.

4. *Persistence of physical, mental, and emotional abnormalities even in the healthiest segment of the population.* Much has been done but much remains to be done to correct these difficulties. From several national sources, common health problems and deficiencies among children seem to occur as follows:

	Percent
Dental problems	50 -90
Poor health habits (rest, diet, and so forth)	20 -30
Visual disorders	10 -15
Emotional problems	5 -10
Mental disorders	5 -10
Nasal obstruction and allergies	6 - 8
Speech disorders	5 - 7
Orthopedic conditions	3 -10
Hearing disorders	2 - 5
Hernia and genitourinary abnormalities	2 - 5
Cardiac conditions	0.4- 1.0
Epilepsy and convulsive disorders	0.5- 1.0
Cerebral palsy	0.1
Diabetes	0.02

These findings give urgency, not complacency, to educators and health leaders. Prompt remedial care can minimize most childhood defects. For instance, it is felt that 80% of the hearing impairments can be cured if found early and given treatment.

5. *Urgent need for more teamwork between educators and those in health and social sciences.* Current educational programs stress that each child should be helped to develop to his maximum. This intensified learning over more years begets serious problems requiring a variety of skills to solve them. Thus, modern school systems employ auxiliary professional workers to aid the educators. Psychologists and social workers, along with health personnel, focus attention on the individual pupil and group problems. A common problem for which parents seek the help of pediatricians or family physicians is that of school failure or underachievement. To help solve such problems, physicians must know the educational system and staff, and the teachers and administrators must appreciate the doctor's role in caring for the child and sharing important insights and suggestions. Excellent teamwork between educators and health specialists is exemplified well by the publication *School Health News* from the Minnesota Departments of Health and Education.

6. *Stronger commitment of parents and communities to improve health of the school age.* Although progress has been made and many diseases controlled, the level of child and youth fitness must be upgraded further. Far too many defects go uncorrected because of parental indifference, ignorance, or lack of funds. School health has been called industrial health for those of school age. Because the pupil-workers are minors and therefore the legal responsibility of their parents, dental and medical care depend on parental understanding and motivation. In some instances communities may lack health resources but usually resourceful schools and social agencies can find funds for treatment and rehabilitation of children if family concern and competence are present.

In conclusion, if these 6 major problems and challenges in school health are to be faced realistically and even partially solved, some changes must be made. Many educators and health personnel are concerned about them already and children and youth will benefit from our continued efforts to improve our programs.

Gastric Carcinoma in an Adolescent

Case Report: Occurrence in a 16-year-old schoolgirl

JAMES R. STONE, M.D., and K. G. VANDERGON, M.D.
Grand Forks

THE OVERALL incidence of carcinoma of the stomach is apparently decreasing. Carcinoma of the stomach in the third decade is not common and in the second decade is rare. The purpose of this report is to record, briefly, the occurrence of this disease in a 16-year-old girl.

CASE REPORT

In June 1964, the patient was first seen because of epigastric pain. Exact onset could not be determined because of insidious onset, although it had probably been present for a month or more. There was no relationship to food, to time of day, or to position. It was, in short, a rather vague pain. Past history was negative, as was family history, except for the fact that her mother and maternal grandmother had multiple sclerosis. Physical examination was negative. The upper gastrointestinal tract X-rays showed "irritable duodenum." Antacids were prescribed which relieved her considerably. In August 1964, she was "doing fine."

She then left for school and was not seen again until February 1965. A feeling of fullness in the upper epigastrium had been bothering her for some time and was becoming worse, especially after meals. Moreover, she was vomiting frequently and had lost 21 lb. since August. Repeat upper gastrointestinal X-rays showed the startling finding of linitis plastica. The stomach was palpated as she stood and leaned forward during fluoroscopy.

At laparotomy the stomach, pancreas, and transverse colon were all involved with tumor. Lymph nodes and liver seemed not to be involved. The stomach, body and tail of pancreas, spleen, part of transverse colon, and some omentum were removed "en bloc." Postoperatively she developed a left pleural effusion which has since cleared.

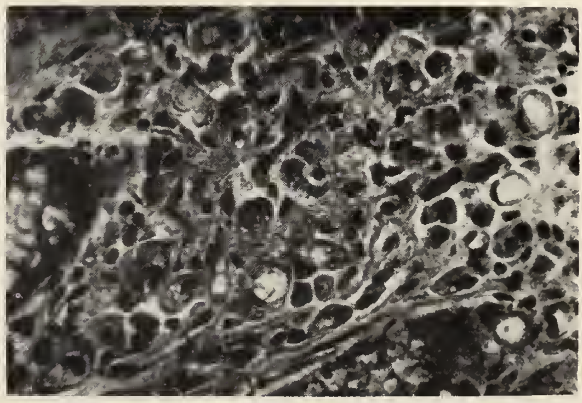
The stomach was narrow, stiff, and rubbery. The wall was uniformly thickened to 1 cm.; one's little finger would barely enter the antrum. A 2 cm. in diameter ulcer crater was found on the greater curvature 5 cm. from the pylorus. A slight depression was noted on the serosa beneath the ulcer and a thin fibrous septum lay between ulcer base and serosa. Microscopically typical desmoplastic tumor was seen infiltrating throughout the stomach wall. Much of the mucosa was intact. Tumor cells were scattered, pleomorphic, and undifferentiated except for occasional signet-ring cells. Fibrous connective tissue reaction was marked. Tumor invasion was noted in sections of the pancreas, colon, and omentum.

CONCLUSION

The occurrence of carcinoma of the stomach in a 16-year-old schoolgirl has been recorded. She has, following surgery, progressed satisfactorily, in spite of which prognosis remains poor.

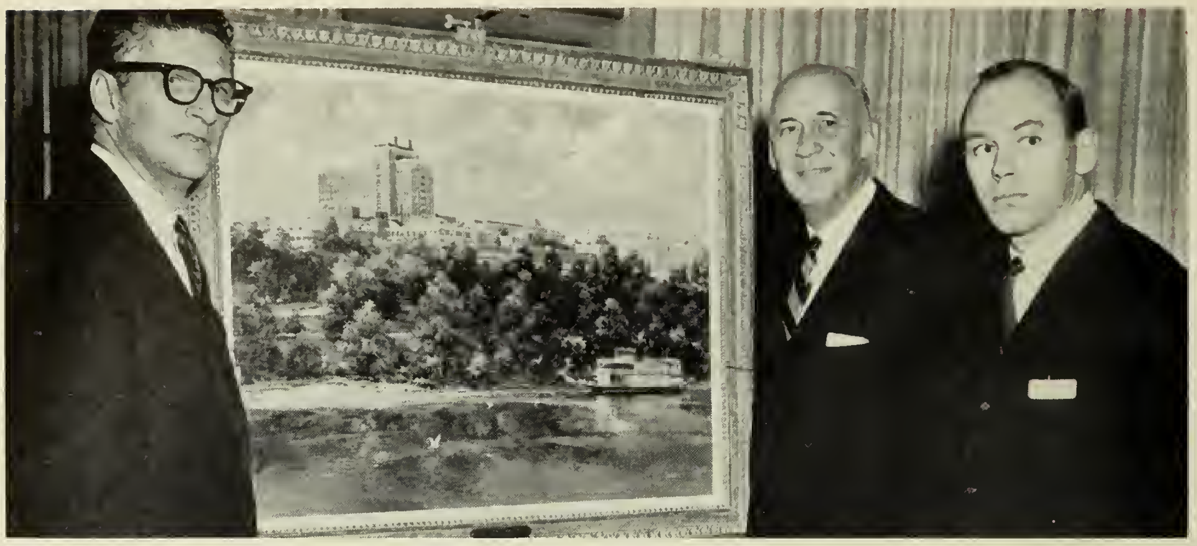
ADDENDUM

The patient died approximately one month after this paper was submitted for publication. Unfortunately, permission for autopsy was not obtained.



Malignant cells in stomach submucosa. A few signet-ring cells can be seen, also.

J. R. STONE *is from the Department of Pathology, University of North Dakota School of Medicine, Grand Forks, and* K. G. VANDERGON *is a general practitioner in Grand Forks.*



Left to right, Dean Robert B. Howard, George S. Squibb, artist John C. Berkey
Painting shows medical school at University of Minnesota

U. of M. Medical School Gets Painting of Campus

The University of Minnesota College of Medical Sciences has had its portrait done. An original oil painting of the campus was presented to the school by George S. Squibb, vice-president of E. R. Squibb & Sons, Inc., at a reception and dinner attended by more than a hundred physicians and educators.

After unveiling and presentation ceremonies, the painting was accepted for the school by University President O. Meredith Wilson and Dr. Robert B. Howard, Dean of the College of Medical Sciences.

The painting is the work of John C. Berkey, a prominent Minnesota artist. It shows a view of most of the buildings in the medical complex as they appear from a spot on the opposite bank of the Mississippi river.

The work was commissioned by Squibb as part of the pharmaceutical firm's long-range plan—known as the "Collegia Medica" project—to create a collection of original paintings of all 86 American medical schools.

O. Meredith Wilson
Addresses group

Left to right, Drs. Wallace D. Armstrong, Jay A. Myers, Maurice B. Visscher, and C. Walton Lillehei. Faculty members chat at reception in Coffman Memorial Union.

Coronary Artery Disease Among the Miskito Indians: Preliminary Report

SAMUEL B. MARX, M.D., and LESTER E. WOLD, M.D.

Rio Coco, Nicaragua, and Fargo

TWO YEARS AGO it was my privilege to spend two months visiting a medical missionary friend, Dr. Sam Marx. This dedicated physician, who is also an ordained minister, has been a medical missionary to the Miskito Indians in Honduras and Nicaragua for the past decade. During the time that I visited Dr. Marx, I was impressed with the fact that I saw no one who clinically had angina pectoris. Upon returning home, I asked the North Dakota affiliate of the the American Heart Association if they would underwrite a project of obtaining consecutive electrocardiographic tracings on Miskito Indians over the age of 50 in an attempt to determine whether there was any electrocardiographic evidence of coronary artery disease in this rather primitive group of people.

An instrument was provided and consecutive tracings taken on all male Miskito Indians over the age of 50 who came to Dr. Marx's clinic for any reason whatsoever. Unfortunately, Dr. Marx was transferred to Bilwaskarma, across the border in Nicaragua from his original location in Ahuas, Honduras, after only 40 such tracings were taken. It is our hope that this study will continue in his new location. At the present time, however, there are some technical problems involved in the operation of the electrocardiograph machine. Because of difficulties in communication, these have not yet been straightened out nor does it appear that they will be for the next several months. Consequently, this is a preliminary report on the study.

In times past, the Miskito[1] people of Honduras and Nicaragua lived in huts, sometimes communal, built with a thatched roof, low eaves, and no sides. The beds were four posts in the ground with a covering of split bamboo on the cross pieces. Nowadays, the majority of the houses have split bamboo or hand-cut board sides and most have a floor elevated about 3 or 4 ft. from the ground. Their clothes were simply a piece of bark cloth as a loin cloth for the men and a long strip of the beaten bark cloth wrapped around the torso of the women.

In their houses they usually only had low wooden stools with three or four legs and a flat or concave surface, cut directly from a trunk or block of wood. The most prized possession of those who had one was a wooden chest or trunk, usually made of cedar or mahogany. The lighting at night was a pile of pine knots burning on the ground. The stove was simply a corner of the house or else a slightly elevated ground platform. Three green logs were used as the support for the round cast iron cook pot in which the bananas, cassava, or sweet potatoes were cooked.

Other equipment in most homes was a mortar and wooden pestle used to pound the hull off the rice or grind other foods. Foods were served in large calabashes split in half and hollowed out. Other calabashes with only one hole in the end served for carrying water from the creek or river. Fermented drinks were stored in earthen vessels, wooden casks, or else segments of large bamboos. In the kitchen corner of the house a loosely woven net held a large wooden spoon, the calabashes, and a 2- or 3-ft. long wooden pestle used to mash the bananas for the "wabul." Rough leaves of a small tree (Curatella americana L.) were used for polishing purposes.

Cutting elements of days gone by as today were the machete, the axe, the adz, and small knives. For hunting, muzzle-loading guns and bows and arrows were used. Formerly, the Miskito people were very warlike, subjugating the Sumu and Paya Indians.

Many of these same conditions still exist today, especially in the outlying villages, except that all now have imported cloth clothing. Most homes have plates and cups bought in some shop, al-

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SAMUEL B. MARX *is at Hospital Thaeler Memorial, Rio Coco, Nicaragua, and* LESTER E. WOLD *is with the Fargo Clinic.*

Type of tracing	*No.*	*Distribution*
Normal	24	
Probably normal	2	1-Slight S-T elevation, lead II with some clockwise motion 1-Slight S-T segment elevation lead II, AVF, V_5, and V_6
Within normal limits	4	2-Slightly low in lead I 1-Sinus tachycardia 1-Slightly low voltage
Borderline	3	2-Low voltage with clockwise rotation 1-Low voltage
Abnormal	7	2-Nonspecific changes. One digitalis effect and one flat T in leads I, II 1-Incomplete bundle branch block 1-Low-voltage atrial ectopics with bigeminy 2-Atrial fibrillation 1-Complete bundle branch block

though they still continue to use the calabash, too. The diet mainstay is still the banana or cassava mash with meat once or twice a week, depending on how often fresh meat is available or wild meat is brought from the hunt. In the dry season, there are usually more fish and seafoods also available, as well as turtles, iguana, and sea turtle eggs. Now, some also buy a little flour, sugar, and cooking fat to make bread.

So you see, actually the Miskito folks around Ahuas sometimes eat a lot of meat, fiish, and eggs. They try to have meat once a day and occasionally, as often as 3 times a day. They eat a lot of cooked bananas, cassava, and sweet potatoes. They like salt but often do not have very much of this seasoning. They like fried foods but, because of the scarcity of fat for frying, enjoy this type of food preparation only occasionally. Most of the meat is cooked, sometimes roasted. They usually fry bananas and a kind of pancake made without baking powder.

Many of the men and women smoke, but except for the young men, this is usually a pipe. The day usually starts at daybreak or before, but they are in bed early except when there is moonlight when they can go visiting.

It is customary for the mothers in this part of Honduras to nurse their children until they are two or three years of age. During childhood, the children only rarely have any cow or goat milk. The mainstays in the diet are beans and rice.

Many men go away to work up the coast, in the gold mines, or at the shrimp plant, indeed anywhere where work is available. Most return home in a year or two; a few never return.

All of the electrocardiograms in this study were interpreted by Dr. Matt Ehlen of the Department of Internal Medicine at the Fargo Clinic (see Table). His report of the tracings is as follows: twenty-four were completely normal Two were probably normal, and of these two, one showed slight S-T elevation in lead II with some clockwise rotation. A second tracing showed slight S-T segment elevation in lead II, AVF, V_5, and V_6. Four tracings were within normal limits. Two of these showed the T wave to be slightly low in lead I. One had a sinus tachycardia and one had a slightly low voltage. Three of the tracings were borderline, according to Dr. Ehlen's interpretation. Two of these showed low voltage with clockwise rotation and one showed low voltage. Seven of the tracings were abnormal. Two had nonspecific changes, and in one of these two instances, there was slight S-T depression in lead II, AVF, V_3, V_4, V_5, and V_6—digitalis effect. The other had a flat T in leads I and II. A diphasic T was noted in AVL and clockwise rotation was also reported. One tracing was abnormal in that it had an incomplete left bundle branch block. One tracing revealed a complete right bundle branch block. One tracing was abnormal in that it had low-voltage T waves; atrial ectopics with bigeminy were reported. There was a single atrial ectopic with aberrant conduction. Two tracings showed atrial fibrillation.

SUMMARY

A series of forty consecutive tracings on Miskito Indians over the age of 50 were studied. Thirty of these tracings were reported as normal. Two were probably normal, and four were within normal limits. Three were borderline and seven were abnormal. None of the abnormal tracings were diagnostic of a prior myocardial infarction.

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Donald W. Hastings, M.D.

BURTRUM C. SCHIELE, M.D.
Minneapolis

DONALD W. HASTINGS, head of the department of psychiatry and neurology at the University of Minnesota Medical School, recalls that he was made dramatically aware of the urgent need for advances in training and research in the field of psychiatry when he served as chief psychiatrist to the Eighth Air Force during World War II. He was stationed in England at the time and carried a heavy load of administrative and clinical responsibility for the welfare of the personnel that manned the largest U.S. heavy bombardment force. There Dr. Hastings saw firsthand what was to become a commonplace thing among psychiatric armed forces staff—that not only was the number of men rejected from the military for psychiatric reasons alarmingly high, but the number later released from duty because of psychiatric disabilities exceeded the numbers released for all other medical reasons combined. Dr. Hastings gained knowledge of the effects of severe emotional stress on carefully selected, trained men who suffered not only from fatigue and strain of bombing missions but also from knowledge that chances of surviving 25 missions required for rotation were slim. He also noted a high incidence of disabling anxiety in men who survived at the expense of their replacements.

These experiences and observations impressed on Dr. Hastings the need for improving the training of physicians in psychiatry, especially when he saw that many of the doctors attempting to treat psychiatric war casualties were not equipped to do so. The majority of wartime psychiatric disorders were not psychotic but were a form of neurosis or psychosomatic disorder. This reinforced his belief that not only must general psychiatric training in the medical schools be improved, but that particular stress should be given to teaching the diagnosis and management of psychosomatic disorders.

Because he had proved both his clinical aptitude in treatment of war neuroses and administrative ability in setting up treatment centers, Dr. Hastings was 1 of 3 officers chosen by the Air Force to set up Don Cesar Hospital in St. Petersburg, Fla., for the treatment of flying personnel. His continued success in this endeavor led to his appointment as chief psychiatrist of the Air Force and, as such, his subsequent mission to Saipan and Leyte to study methods to minimize the psychopathological impact of combat.

Dr. Hastings was born and educated in Madison, Wis., where his father was a business executive. During his undergraduate years at the University of Wisconsin, he had a number of contacts with people in medicine, which probably attracted him to the field. He lived next door to a physician who was a close friend, and for 5 summers he worked as an orderly in the local hospital. After he graduated from the University of Wisconsin Medical School with honors in

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BURTRUM C. SCHIELE *is a professor at the University of Minnesota, Minneapolis.*

1934, he interned at Philadelphia General Hospital and took his residency at the Philadelphia Hospital for Nervous and Mental Diseases and the Institute of Pennsylvania Hospital, at both of which he had a Rockefeller Fellowship in psychiatry. During this period he married Jane Wenban and took her to Harvard with him, where he spent the third year of his residency doing research in "normal" personalities. At Harvard, he recalls, one of the sophomore students who passed tests that proved him to be a superbly well adjusted individual was John F. Kennedy. Dr. Hastings returned to Philadelphia after a year to take an appointment as clinical director of the Pennsylvania Hospital of Nervous and Mental Diseases. At the outbreak of the war he was one of the few civilians to go through the School of Aviation Medicine at Randolph Field, Texas. He received his commission at the termination of this course of instruction and was shortly thereafter sent overseas as chief of psychiatry to the Eighth Air Force. At the close of this distinguished episode in his career, he was discharged at the request of the University of Pennsylvania (on the day the atomic bomb was dropped on Hiroshima), but his stay in Philadelphia was brief, for he soon was called to chair the University of Minnesota department of psychiatry and neurology in March 1946.

Dr. Hastings, throughout his entire professional career, has also had a very happy family life, spending much time in family activities with his wife and 3 children; these activities include, among others, travel, skiing, sailing, and fishing. During his undergraduate years at Wisconsin he was captain of the rifle team. His marksmanship is unimpaired, as his hunting companions will testify. His wife goes on some of his hunting trips, even though music is her main interest. He, in turn, occasionally tries the organ.

As an administrator, Dr. Hastings is a man of unfailing good nature and generosity, which makes him pleasant to work with and be around. He is relaxed, calm, self-assured, even tempered and tolerant, and he shows great breadth of vision when confronted with administrative problems. He is singularly unthreatened when members of his staff disagree with him and often shifts his viewpoint or acquiesces, depending on the merits of the argument presented. As a teacher and writer he has a very clear and lucid style and is easy to listen to and read.

Since his appointment at the University of Minnesota, his department has prospered and grown, for which Dr. Hastings deserves a great deal of credit. The chief effort during his first ten years was to build the teaching staffs of the various divisions and to modernize the undergraduate teaching program, which had been too heavily weighted toward neurologic and organic disorders. He devoted major energy in the next decade to the reorganization of the department, which had formerly been the department of neuropsychiatry, and to realizing the research potential of the department's 4 divisions: neurology, adult psychiatry, child psychiatry, and psychology. Tangible evidence of their research activity is provided by the amount of current research grants, which now totals more than $880,000 annually, and the new laboratories in Diehl Hall for psychiatric and neurologic research completed in the summer of 1964.

A less tangible but possibly more important contribution to the department's growth in teaching and research has been Dr. Hastings' talent for creating an atmosphere in which staff members have found it possible to develop various potentials. Dr. Hastings is the kind of administrator who fosters growth in others.

Dr. Hastings' personal accomplishments in his chosen field are varied and cover several areas. Early in his career he began to show an interest in new techniques and knowledge in the field of psychiatry, as well as in mastering all the standard techniques. His early publications, written during and immediately after his residency, concerned themselves with the then new physiological therapies. He pursued this interest and has published a number of articles on these therapies, including insulin shock, metrazol therapy, electroshock, and sodium amytal narcosis. General publications include his contribution to a book on his experiences as a psychiatrist in the Air Force, an article on the future of psychiatry, and a number of articles on psychosomatic problems in general medicine. He has also written on differential diagnosis of brain tumor, somatopsychic disorders of old age, the psychiatric problems of mental deficiency, the psychiatric problems of criminal rehabilitation, the prognostic factors in schizophrenia, and the clinical management of depression. Currently, one of Dr. Hastings' major interests is psychological impotence and frigidity. He just published a definitive and well written book on the subject aimed at the general physician. As he approaches his twentieth year in his present post, he must be gratified not only by the long list of his personal accomplishments, but also by the flourishing clinical, teaching, and research programs in all the divisions of his department.

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Book Reviews . . .

The Obstructing Acromion: Underlying Diseases, Clinical Development, and Surgery

by BERNARD DIAMOND, M.D., *212 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $9.50*

Dr. Diamond reviews his personal experience with 44 patients in whom surgical resection of the acromion of the shoulder was deemed necessary for disorders in the subacromial region. His conclusions are that the procedure is rational, useful, and safe. All the patients improved. Of the 38 patients who could be examined for long-term evaluation, there were no unsatisfactory results, except in one patient in whom wound infection resulted in disfigurement. Dr. Diamond feels that the surgeon's fear of operation is unwarranted and that the procedure should not be withheld from patients who suffer painful, disabling lesions of the shoulder, unresponsive to conservative treatment.

The operation which Dr. Diamond describes is one of vertical splitting of the deltoid and trapezius muscles in the line of the fibers, separating the muscles from the acromion process, without detaching the deltoid muscle in the saggital plane, as is commonly done for acromial resection. He feels this avoids the troublesome problem, seen in other types of operations, of reattaching the deltoid to the shoulder. His operation allows early postoperative motion which is necessary for restoration of function. By doing an incomplete or subtotal resection and leaving the posterior angle of the acromion as a protecting shelf, Dr. Diamond avoids the possibility of the humerus dislocating upward. The procedure is well illustrated and described. There are many excellent illustrations throughout the text. Dr. Diamond was most fortunate in securing Daisy Stilwell to do the illustrations. A simple, slanted board support, helpful in positioning the patient for surgery, is described and illustrated.

Dr. Diamond agrees that 44 cases is not statistically large, but this represents a considerable experience with shoulder disorders, most of which have been treated conservatively. As indications for surgical resection of the acromion, Dr. Diamond mentions 3 main categories: the recalcitrant subacromial lesion that causes obstruction, the necessity for removal of extensive diseased tissue in the area, and the need for securing complete access to the shoulder. In concise tables in the appendix, Dr. Diamond lists his cases under the headings of: Chronic Calcified Tendinitis; Chronic Lesions of Bursa, Biceps and Supraspinatus; Chronic Ordinary Cuff Tears; Chronic Massive Cuff Tears; Greater Tuberosity Fractures; and Elongated Acromion of Birth Palsy. There are also many comments based on observation and diagnosis of shoulder disorders.

The difficulties of diagnosis and differential diagnosis of shoulder diseases and the frequently unhappy results of treatment have engendered a well-merited respect for the shoulder by all doctors. As an accounting of operative treatment, the book can be profitably read, especially by the orthopedic surgeon. The book is not well organized and is quite rambling, but this does not detract from its interest. Dr. Diamond does not mention the work of Dr. T. T. Stamm of London, but it is worth

(Continued on page 14A)

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(Continued from page 12A)

noting. Dr. Stamm attacks the problem by lowering the glenoid and humerus away from the acromion by means of an osteotomy through the neck of the scapula and reports good results.

JOHN F. POHL, M.D.
Minneapolis

Anticoagulant Therapy in Ischemic Heart Disease

edited by E. STERLING NICHOL, M.D., *et al., 469 pp., Grune & Stratton, Inc., New York City, 1965. $10*

In January of 1964, the Miami Heart Institute sponsored a symposium on "The Use of Anticoagulant Therapy in Ischemic Heart Disease." The papers presented at this symposium have been collected and bound together in a volume entitled "Anticoagulant Therapy in Ischemic Heart Disease."

The list of contributors contains the names of a great many investigators and clinicians well known in the field of anticoagulant therapy and both proponents and opponents of this controversial form of treatment present their views. Both heparin and oral anticoagulation is discussed in detail and thrombolytic therapy is touched upon.

As might be expected, a number of series are presented, most of these well controlled, with conclusions drawn from these. The problems of acute myocardial infarction, impending infarction, and long-term anticoagulation are all discussed in detail. Several excellent papers are pathologically oriented, and a number of other papers concern themselves primarily with the physiology and chemistry of clothing and the mechanisms of anticoagulation.

The book is clearly printed and the format is that of the journal "Circulation." Most of the ideas presented have been published before by these authors, but the current papers have been brought up-to-date and broadened in their scope. One would have to search many journals published over the past ten years or more in order to find all the material herein collected. This book, as of 1965, certainly contains the best of what is known about anticoagulants in ischemic heart disease and would be a valuable addition to the library of any physician who treats this disorder.

MILTON M. HURWITZ, M.D.
St. Paul

Neurological Surgery of Trauma

prepared and published under the direction of LT. GEN. LEONARD D. HEATON, *editor-in-chief,* COL. JOHN BOYD COATES, JR., *and edited by* ARNOLD M. MEIROWSKY, M.D., *604 pp., ill., Office of the Surgeon General, Department of Army, Washington, D.C., 1965. $6.25*

This book is about wartime trauma to the central and peripheral nervous system. The special value of the book lies in the reporting of personal experience by individual neurosurgeons and neurologists working in the Korean theater of operations. It is edited by Dr. Arnold Meirowsky, who had incomparable military experience in that war. The fact that Dr. Meirowsky is the editor, along with his own authoritative chapters, makes it a valuable volume.

The book is divided into 4 general areas of interest:

1. Military neurosurgery, in which those elements peculiar to wartime injuries are stressed (basically, an introduction for later chapters).

2. Craniocerebral trauma, including differential diagnosis, treatment of acute and chronic lesions such as cerebrospinal fluid fistula, cranial defects, and epilepsy, and a step-by-step outline of surgical procedures.

3. Trauma of the spinal cord in which physiologic mechanisms responsible for neurological signs and symptoms are nicely outlined. There is a comprehensible chapter on physical and vocational rehabilitation. There are also chapters on the lumbar, thoracic, and cervical intervertebral disks, written in the light of civilian experiences which are maturely produced.

4. Peripheral nerve lesions including chapters on diagnosis, techniques of surgery, and prognosis which are superior. Of particular interest is the lucid, well illustrated discussion on testing of specific muscle functions.

The book is adequately illustrated. The line drawn illustrations of operative techniques and the black and white photographs are especially good. It is printed on high quality paper and the binding is excellent. In addition, there are some chapters which are largely on civilian experiences which help to convert the comparatively rigid concepts of wartime surgery to those used in peacetime.

The book is recommended for all surgeons who encounter problems on trauma of the nervous system.

LYLE A. FRENCH, M.D.
Minneapoilis

Chemistry and Treatment of Adrenocortical Diseases

by F. T. G. PRUNTY, M.D., *380 pp., ill. Charles C Thomas, Springfield, Ill., 1964. $14*

This book is a monograph in the series "American Lectures in Living Chemistry," and is concerned primarily with the biochemical derangements underlying the clinical disorders of the adrenal cortex in man. The first one-third of the book is devoted to the discussion of the synthesis of adrenal steroid, the control of adrenal hormone release, the metabolism of adrenal steroids, including aldosterone, the actions and effects of adrenal steroids and the basis for steroids estimation, transport, and use in the diagnosis of adrenocortical disease. The last two-thirds of the book presents a very clear and comprehensive discussion of the use and interpretation of steroid chemistry in the diagnosis of adrenocortical hyper- and hypofunction. Also included is a chapter on primary aldosteronism. Some discussion of the treatment of adrenocortical disease is also presented.

Although the steroid chemist and research endocrinologist might find the monograph somewhat superficial in its treatment of steroid biochemistry, the material presented is very adequate for the clinical endocrinologist and other clinicians who encounter patients with adrenocortical disease. The author makes a continual effort to correlate abnormal biochemistry with the clinical findings so that the text is directed mainly at the clinician seeing patients rather than the laboratory investigator.

This book will be a valuable addition to the library of the clinician both as a short course in adrenocortical biochemistry and also as a reference text in the management of patients. A comprehensive bibliography is included so that reference to the original literature can be made. Certainly every endocrinologist will find this book of great interest and clinicians in the field of general medicine would also find it useful.

ALVIN L. SCHULTZ, M.D.
Minneapolis

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News Briefs . . .

North Dakota

DR. GEORGE H. HALL, JR., has been elected president of the St. Lukes Hospital medical staff in Fargo. Dr. Hall is a member of the American Board of Surgery and the American College of Surgeons. He received his medical degree from the University of Minnesota Medical School in 1939.

* * * *

DR. JAMES J. MOSES of Bismarck has received his specialty certification from the American Board of Urology. Dr. Moses is with the Quain and Ramstad Clinic. He is a graduate of the Bowman Gray School of Medicine, Winston-Salem, N.C.

* * * *

DR. GORDON B. MAGILL has been elected chief of the medical staff at St. John's Hospital, Fargo. Dr. Magill received his medical degree from Columbia University, N.Y., and is a member of the American Society of Internal Medicine and the Aerospace Medical Association.

* * * *

DR. EDWIN G. RICE has joined Dr. Ernest L. Grinnell in practice at Grand Forks Clinic. Dr. Rice received his degree from the University of Washington, Seattle, in 1960.

* * * *

DR. CLIFFORD H. PETERS of Bismarck has been elected president of the board of directors of the Heartview Alcoholism Treatment Center of Mandan.

* * * *

DR. MARY E. OBERT of Fargo has been named Cass County superintendent of public health. She and her husband, Dr. Gerald J. Obert, previously were in private practice in Grand Forks.

* * * *

DR. RIFAAT F. MORGAN has joined St. Alexius Hospital in Bismarck as director of the department of anesthesiology and the Central North Dakota School of Anesthesiology. His wife, Dr. Margaret E. Morgan, has been appointed associate anesthesiologist at St. Alexius. Both were associated with the University of Pennsylvania before coming to Bismarck.

* * * *

DR. RAYMOND L. COULTRIP, JR., a general practitioner from McVille, is organizing a health training program for the care of civilians in Phouctuy Province, Vietnam.

* * * *

DR. LESTER D. SHOOK, head of radiology at the Fargo Clinic and St. Lukes Hospital, has been named a fellow of the American College of Radiology. Dr. Shook received his degree from the University of Illinois College of Medicine and is a member of the American Board of Radiology and the Radiological Society of North America.

* * * *

DR. PETER V. MORRISON has started a general practice in Towner. Dr. Morrison has practiced in Saskatchewan since receiving his medical degree in London, England, in 1962.

* * * *

DR. WILLIAM M. GOODALL will be associated with Dr. Nicholas Kaluzniak of Langdon after completing his internship at Winnipeg General Hospital in June.

* * * *

DR. LEONARD KLASSEN has joined Drs. Stuart J. Cook and

John Sawchuk at the Rolette and Dunseith Medical Clinics. Dr. Klassen is a graduate of the University of Alberta School of Medicine.

* * * *

DR. JAMES G. ALLARDICE from Weyburn, Saskatchewan, has started medical practice in Stanley in association with Dr. William D. LaRochelle at the Stanley Clinic. He received his medical degree in London, England, in 1958.

* * * *

DR. MICHAEL P. RIISAGER has joined Drs. Thomas F. Gibson and Shelagh M. Milligan in their practice at Mandan. Dr. Riisager arrived from England in November.

Minnesota

DRS. WILLIAM E. MAYBERRY and HOWARD F. TASWELL of the Mayo Clinic have received Public Health grants totaling approximately $36,000. Dr. Mayberry, a specialist in metabolism, received $21,632 for research in the formation of thyroxine, and Dr. Taswell, a clinical pathologist, received $14,233 for research in preventing hepatitis after cardiovascular surgery.

* * * *

DR. JOHN R. FISCHER has closed his office in Blooming Prairie in order to continue his training at the Washington University School of Medicine, St. Louis, Mo.

* * * *

THE E. G. NETHERCOTT MEDICAL EDUCATION FOUNDATION has been established as a memorial to the former Pine City physician. An announcement from his widow said the foundation would assist students seeking education and training in medical and paramedical fields.

* * * *

DR. RICHARD E. BARTMAN, director of children's mental health services in the State Department of Public Welfare, has resigned to become assistant superintendent of Sonoma State Hospital, Eldridge, Calif.

* * * *

DR. JAMES JANECEK, assistant professor of psychiatry at University of Minnesota Hospitals, has joined the staff at St. Paul–Ramsey Hospital as director of psychiatric inpatient service.

* * * *

DR. LAWRENCE R. GOWAN, JR., has been named consulting psychiatrist for the University of Minnesota at Duluth health service.

* * * *

THE MAYO CLINIC AND MAYO FOUNDATION have announced a ten-year, $25 million building program which will add eight stories to the present clinic by 1969. The addition will turn the clinic into a 19-story building. A $6 million laboratory for teaching and research will be built near the present complex.

* * * *

DR. ELTON G. WING, a former resident of Jackson, will join Dr. Elmer E. Keithahn in a new clinic at Sleepy Eye after completing his internship at Ancker Hospital, St. Paul.

* * * *

DR. CLIFFORD R. MYRE, Paynesville, announced his retirement from active practice and said he would devote full time to cancer research and medical writing. Dr. Myre graduated from the University of Minnesota Medical School in 1924 and had practiced in Paynesville for forty-one years.

* * * *

DR. JAMES ROGERS FOX, Minneapolis internist, has been cited by the American Association for Health, Physical

(Continued on page 18A)

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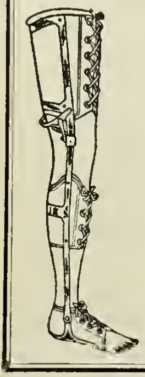

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NEWS BRIEFS

(Continued from page 17A)

Education, and Recreation for his contributions to athletics and health. Dr. Fox produces the "Doctor's Housecall" series for radio and television.

* * * *

DR. GEORGE H. MARKING has been elected president of the medical staff at Swedish Hospital, Minneapolis. Dr. William H. Anderson, Edina, was named president elect, and the new secretary-treasurer is Dr. Markle Karlen of St. Louis Park.

* * * *

THE MEDICAL STAFF at Springfield Community Hospital has been reappointed. Members are Drs. Donald E. Wohlrabe, Edwin J. Wohlrabe, E. Louis Penk, and Francis J. Boyle.

South Dakota

DR. NERE J. SUNDET of Kadoka has been elected to membership in the American Academy of General Practice.

* * * *

DR. HAROLD J. MACDONOUGH, radiologist, has joined Drs. Paul V. McCarthy and Paul R. Leon in private practice at Aberdeen. Dr. MacDonough received his medical degree from the University of Amsterdam, the Netherlands.

* * * *

AN APPEAL for drugs and other products to aid the civilian population of South Vietnam was made to South Dakota physicians by Dr. Robert H. Hayes, a former Winner pediatrician. Dr. Hayes, now with the Public Health Service, is past president of the South Dakota State Medical Association. The first request brought $650 worth of drugs.

* * * *

DR. FREEMAN G. GILBERT of Belle Fourche has joined the staff at the Veterans Administration Hospital, Fort Meade. Dr. Gilbert, a graduate of Loma Linda University School of Medicine, has been a practicing physician in Belle Fourche for twenty years.

* * * *

DR. ROGER HERBRANDSON, a graduate of the University of Minnesota Medical School, has opened practice in Vermillion. He is a native of Alcester.

Deaths . . .

DR. ALFRED L. LINDBERG, 72, general practitioner at Wheaton from 1924 to 1961, died Feb. 10. Dr. Lindberg received his medical degree from the University of Minnesota Medical School in 1923.

* * * *

DR. ALBERT L. PERTL, 66, general practitioner in Canby for thirty years, died Feb. 12. Dr. Pertl was a 1928 graduate of the State University of Iowa College of Medicine and a member of the American Academy of General Practice.

* * * *

DR. JOHN J. HOCHFILZER, 75, otolaryngologist at St. Paul-Ramsey and Miller Hospitals and clinical professor emeritus at the University of Minnesota Medical School, died March 12 while on a skiing vacation in Colorado. Dr. Hochfilzer was a member of the American Board of Otolaryngology, the American Academy of Opthalmology and Otolaryngology, and the American Laryngology, Rhinology, and Otology Society.

* * * *

DR. GEORGE L. JOYCE, 64, deputy coroner at Rochester, died March 8. Dr. Joyce had been a private practitioner in Rochester since 1935. He received his medical degree from Stritch School of Medicine, Loyola University.

* * * *

DR. EDWARD E. NOVAK, 92, a general practitioner at New Prague for seventy years, died March 7. He was a former member of the Minnesota Board of Regents. Dr. Novak began his practice in New Prague in 1895, shortly after graduating from the State University of Iowa College of Medicine.

* * * *

DR. MERRILL A. HOWARD, 69, retired St. Paul practitioner, died March 1. Dr. Howard received his medical degree in 1922 from the University of Minnesota Medical School.

* * * *

DR. LAWRENCE J. KAASA, 86, retired Albert Lee physician, died Feb. 22. He was a former staff physician at the Veterans Administration Hospital, Fort Snelling, and was a member of the staff at St. Peter State Hospital at the time of his retirement in 1956. Dr. Kaasa was a graduate of the State University of Iowa College of Medicine.

* * * *

DR. ELWYN R. HUDEC, 55, of Echo, died March 10. Dr. Hudec, a general practitioner since 1938, was mayor of Echo. He was graduated from the University of Minnesota Medical School and was a member of the American Academy of General Practice.

* * * *

DR. EDWARD CARR ROSENOW, internationally known bacteriologist, died March 7 in Minneapolis. He was 90. Dr. Rosenow founded the experimental bacteriology division at Mayo Clinic in 1915 after eleven years of research work at McCormick Memorial Institute in Chicago. In 1913, he authored a paper on the transmutation of streptococci and pneumococci and a year later contributed one of the earliest enunciations of the theory of focal infection. His research at Mayo ranged from endocarditis and rheumatism to encephalitis and polio, and in 1934 he reported the effective use of a blood serum from horses in preventing paralysis during a polio outbreak in Cuba. Dr. Rosenow was graduated from Rush Medical College in 1902.

* * * *

DR. FREDERIC E. B. FOLEY, 74, St. Paul urologist, died March 24. He had practiced in St. Paul from 1922 to 1960. Dr. Foley was a graduate of Johns Hopkins University School of Medicine and was clinical professor of urology at the University of Minnesota until 1957. His Foley catheter, developed in 1929, was widely used in the surgical treatment of the prostate gland. Dr. Foley was a recipient of the Francis Amory Septennial award from the American Academy of Arts and Sciences for outstanding contributions to urology.

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ECONOMICAL since the average dosage requires only one enema daily for 2 or 3 weeks, then one every other day until remission is established. The selection of Hydrocortisone permits lower patient cost without sacrificing efficacy.

1 Sherman, L. F.: Minnesota Med 48,605 May, 1965. 2 Sherman, L. F. Personal Communication.

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Each 60 cc. unit contains:

Hydrocortisone..100 mg. in aqueous, isotonic saline containing methylcellulose as a suspending agent and emollient; polysorbate 80, and 0.18% methylparaben and 0.02% propylparaben, as preservatives.

Description: CORTENEMA Hydrocortisone Retention Enema is a completely disposable, single-dose unit consisting of a flexible plastic container with a lubricated applicator tip for rectal administration. It is designed to permit self-administration and, therefore, it is suitable for both out-patient and hospital use. It also may be diluted with isotonic saline for administration by intrarectal drip.

CORTENEMA consists of a suspension of partially solubilized hydrocortisone alcohol in an aqueous vehicle. Thus, it provides the potent anti-inflammatory effect characteristic of the corticosteroids. Because hydrocortisone alcohol is absorbed to some extent from the colon, CORTENEMA provides both topical and systemic actions.

Indications: CORTENEMA Hydrocortisone Retention Enema is indicated as an adjunct in the treatment of idiopathic nonspecific ulcerative colitis. It is most useful in cases involving the rectum, sigmoid and left colon, where it exerts a topical effect. Due to its systemic action, CORTENEMA has proved effective in certain cases extending to the transverse and ascending colons.

Rectal steroid therapy brings about prompt symptomatic and proctologic remissions in a significant proportion of patients, but it apparently does not alter the recurrent and progressive nature of ulcerative colitis. Therefore, this form of treatment is not recommended for prophylaxis during periods of remission.

Contraindications: Local contraindications to the use of intrarectal steroids include obstruction, abscess, perforation, peritonitis, fresh intestinal anastomoses, extensive fistulas and sinus tracts. Tuberculosis (active, latent or questionably healed), ocular herpes simplex, and acute psychosis are usually considered absolute contraindications to the use of corticosteroids.

Relative contraindications include active peptic ulcer, acute glomerulonephritis, myasthenia gravis, osteoporosis, diverticulitis, thrombophlebitis, psychic disturbances, pregnancy, diabetes, hyperthyroidism, acute coronary disease, hypertension, limited cardiac reserve, and local or systemic infections, including fungal or exanthematous diseases. Where these conditions exist, the expected benefits from CORTENEMA must be weighed against the risks involved in its use.

If clinical or proctologic improvement does not occur within two or three weeks after starting CORTENEMA, discontinue its use.

Precautions: CORTENEMA Hydrocortisone Retention Enema should be administered with caution in patients with severe ulcerative disease because these patients are predisposed to perforation of the bowel wall. In the advanced stages of chronic ulcerative colitis, where there is loss of mucosa, and thickening and fibrosis of the bowel wall, steroid therapy theoretically might hasten deterioration, although this has not been proved with steroids in actual practice.

In severe cases, where surgery is imminent in the absence of marked clinical improvement, it is hazardous to wait more than a few days for a satisfactory response to medical treatment.

Because of the possibility of adrenal insufficiency caused by suppression of the adrenal cortex by glucocorticoids especially after prolonged therapy, it is important that therapy be withdrawn gradually. If the patient is subjected to unusual stress, while on therapy or up to a year after discontinuation of steroids, adequate supportive measures and increased or reinstated systemic steroid therapy are indicated. In the case of surgery, these measures should be continued throughout the pre- and postoperative recovery periods, bearing in mind the possible deleterious effects of corticosteroids on fresh intestinal anastomoses.

Steroid therapy might impair prognosis in surgery by increasing the hazard of infection. If infection is suspected, appropriate antibiotic therapy must be administered, usually in larger than ordinary doses.

General precautions common to all corticosteroid therapy should be observed during treatment with CORTENEMA, including those pertaining to growth suppression in children during prolonged use. Patients should be kept under close observation. If severe reactions or idiosyncrasies occur, steroids should be discontinued immediately and appropriate measures instituted.

If it is necessary to use CORTENEMA in pregnant patients, their infants should be closely observed for signs of hypoadrenalism; and appropriate measures, including administration of corticosteroids, should be instituted if such signs are seen.

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Adverse Reactions: CORTENEMA Hydrocortisone Retention Enema may produce all of the side effects known to occur with other forms of hydrocortisone therapy. These include moon face, buffalo hump, fluid retention, excessive appetite and weight gain, abnormal fat deposits, mental symptoms, hypertrichosis, acne, striae, ecchymosis, increased sweating, pigmentation, dry scaly skin, thinning scalp hair, thrombophlebitis, decreased resistance to infection, negative nitrogen balance with delayed bone and wound healing, menstrual disorders, neuropathy, peptic ulcer, decreased glucose tolerance, hypopotassemia, adrenal insufficiency, necrotizing angiitis, hypertension, pancreatitis and increased intraocular pressure.

In children, suppression of growth may occur. Increased intracranial pressure may occur and possibly account for headache, insomnia and fatigue. Subcapsular cataracts may result from prolonged usage. Long-term use of all corticosteroids results in catabolic effects characterized by negative protein and calcium balance. Osteoporosis, spontaneous fractures and aseptic necrosis of the hip and humerus may occur as part of this catabolic phenomenon.

Where hypopotassemia and the other symptoms associated with fluid and electrolyte imbalance call for potassium supplementation and salt-poor or salt-free diets, these may be instituted and are compatible with the diet requirements for ulcerative colitis.

Dosage and Administration: The use of CORTENEMA Hydrocortisone Retention Enema as an adjunct in the treatment of ulcerative colitis is predicated upon the concomitant use of modern supportive measures, such as blood replacement, rational dietary control, antispasmodics and sedatives, antibacterial therapy, and systemic steroids.

The usual dose is one CORTENEMA Hydrocortisone Retention Enema daily for two or three weeks and every second day thereafter, administered intrarectally in the evening before retiring. Every effort should be made to retain the medication for at least one hour, preferably all night. This may be facilitated by prior sedation and or antidiarrheal medication. If clinical or proctologic improvement fail to occur within two or three weeks, discontinue the drug.

For administration by retention enema, instruct the patient to lie on his left side during instillation. Shake the bottle vigorously to resuspend the insoluble portion of hydrocortisone. Expose the lubricated tip by removal of the protective sheath, grasping the bottle at the neck where it is most rigid. Carefully insert the lubricated tip into the rectum in the direction of the sacrum. Slowly express the contents by compressing the container. After instillation, the patient should remain on his left side for at least 30 minutes, to allow distribution of the medication throughout the descending colon and rectum.

For coverage of more distant segments of the colon, CORTENEMA Hydrocortisone Retention Enema may be diluted to from 100 cc. to 300 cc. with isotonic saline and administered by intrarectal drip.

The duration of treatment is dependent on the degree of response. If a satisfactory response is to be obtained, it usually occurs within five to seven days, as evidenced by a marked reduction of clinical symptoms. Improvement in the appearance of the mucosa, gauged by barium enemas and sigmoidoscopic examinations, may lag somewhat behind clinical improvement. The usual duration of therapy is two weeks, although some cases require therapy for longer periods (up to two or three months). Minimal control of symptoms is an insufficient basis for the prolonged use of CORTENEMA. If there is no clinical or proctologic response within two or three weeks, or if the patient's condition worsens, discontinue the drug.

Because of hydrocortisone absorption, proper precautions against unwanted systemic reactions or side effects should be observed. Symptomatic improvement, evidenced by decreased diarrhea, weight gain, improved appetite, lessened fever, and decrease in leukocytosis, may be misleading and should not be used as the sole criterion in judging efficacy. Actual sigmoidoscopic examination and X-ray visualization are most reliable. Since steroids can inhibit wound healing, enema or drip therapy should not be employed in the immediate or early postoperative period following ileorectostomy.

How Supplied: CORTENEMA Hydrocortisone Retention Enema is supplied in boxes of seven single-dose units.

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1. Collective studies, Department of Medical Research, Winthrop Laboratories.

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The Journal-Lancet

97th Year of Publication

Special Issue

St. Paul–Ramsey Hospital

Treatment of the Patient with Multiple Injuries

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JUNE 1966

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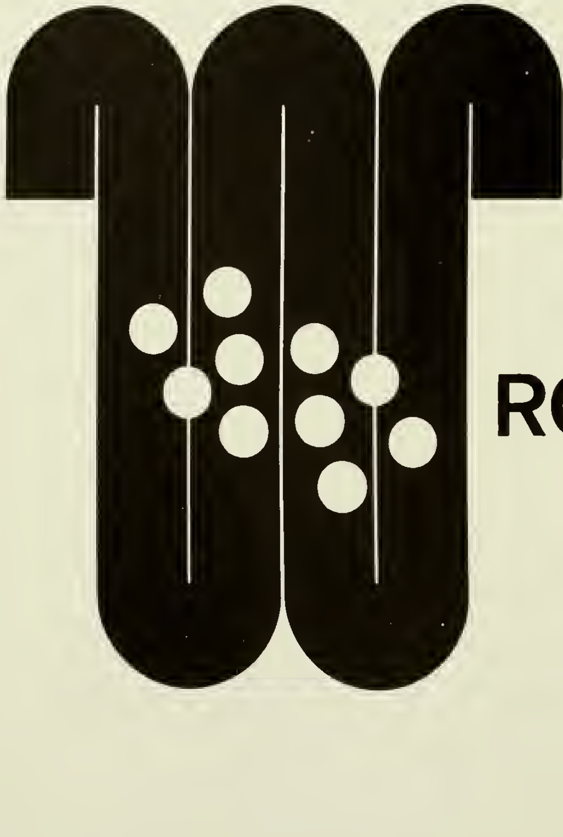

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Contraindications—Pregnancy; organic disease of the central nervous system; evidence or history of blood dyscrasia.

Precautions and Side Effects—Complete blood cell counts should be made before and after therapy, especially if a second course is necessary.

Infrequent and minor side effects include: nausea, unpleasant taste, furry tongue, headache, darkened urine, diarrhea, dizziness, dryness of mouth or vagina, skin rash, dysuria, depression, insomnia, edema. Elimination of trichomonads may aggravate coexisting moniliasis.

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The
Journal-Lancet Volume 86, No. 6, JUNE 1966

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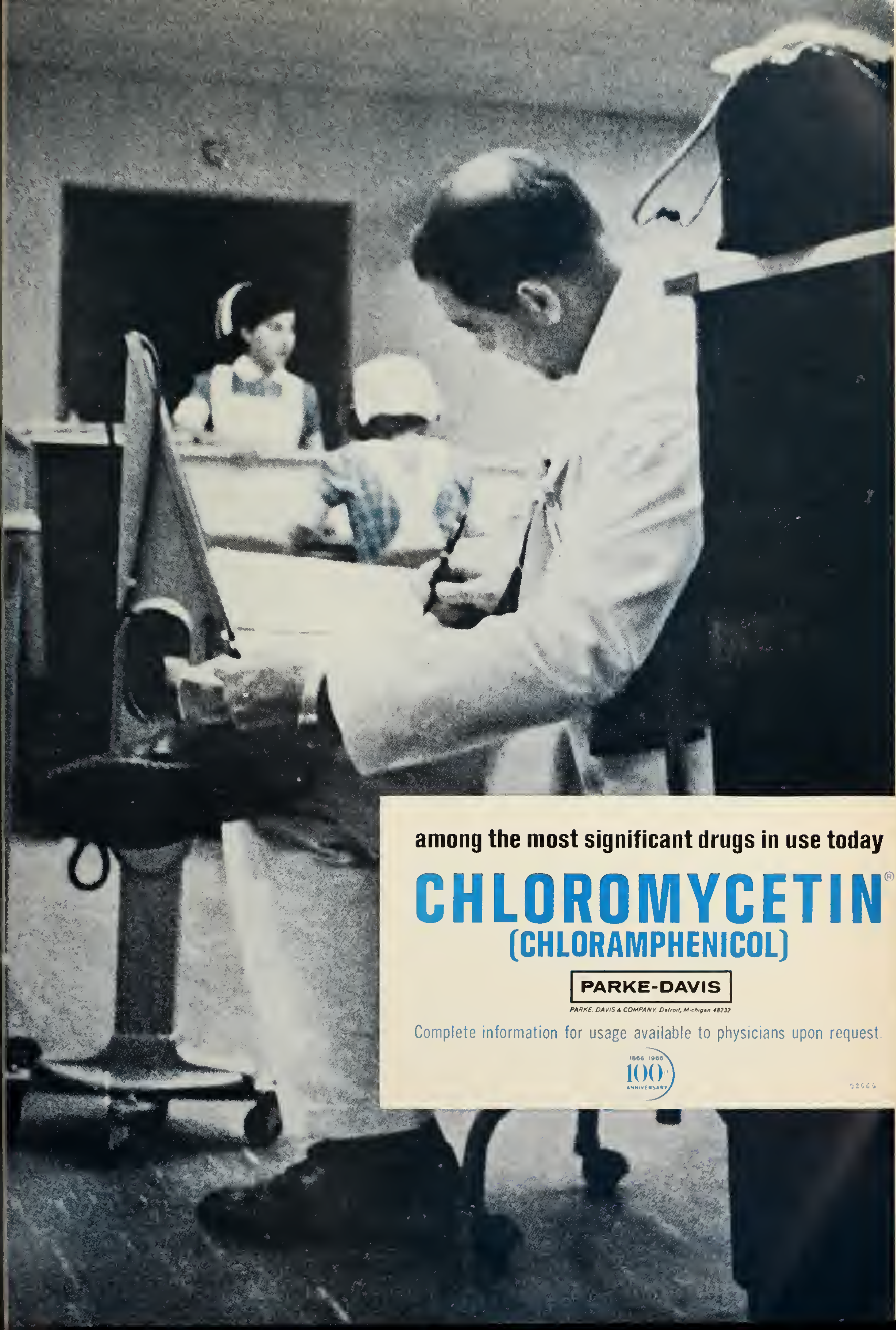

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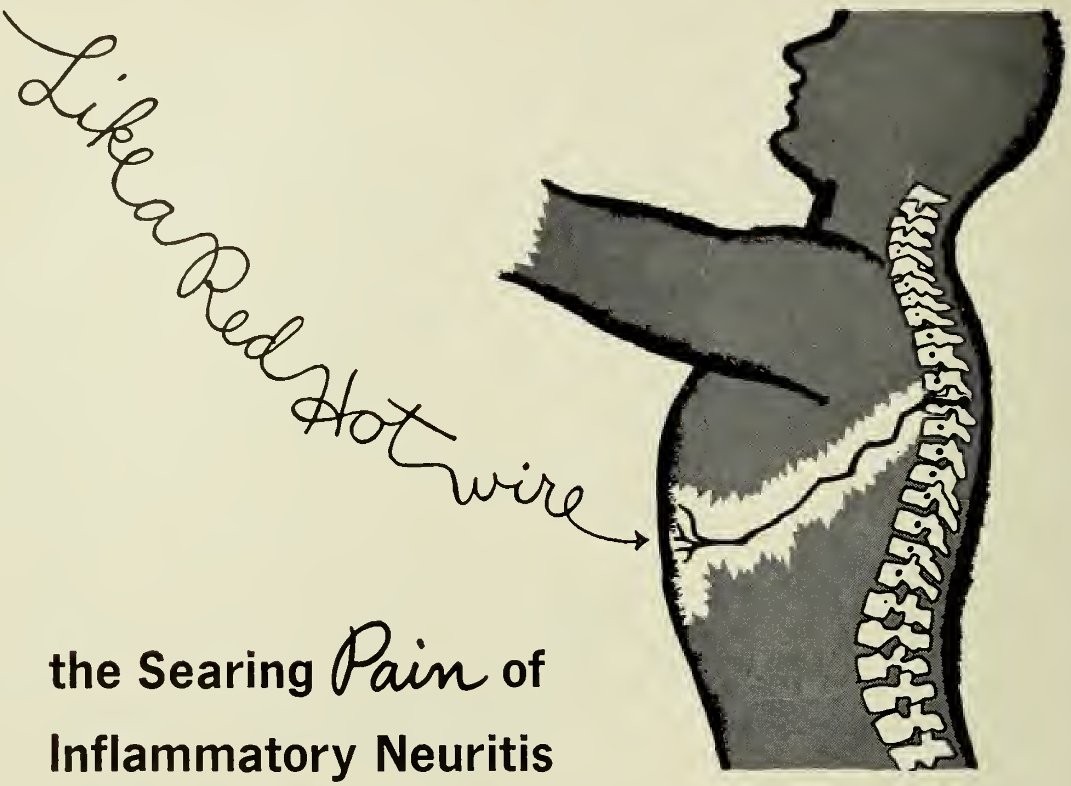
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- **Acute Renal Failure in Childhood,** by Carol R. Angle, M.D.
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- **Psychological Variations in Two Patients with Gonadal Dysgenesis (Turner's Syndrome): Role of the Medical Genetics Counselor,** by Henry T. Lynch, M.D., Thaddeus P. Krush, M.D., Anne J. Krush, M.S., and Robert L. Tips, M.D.
- **Central Language Disorders as Seen in a Mental Retardation Evaluation Clinic,** by Matilda McIntire, M.D., John Wiley, Ph.D., and William Wolski, Ph.D.
- **Congenital Cardiac Defects, a Genetic Viewpoint,** by Paul K. Mooring, M.D., F.A.A.P.
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- **Neonatal Disorders Affecting Subsequent Neurological and Psychological Development,** by Richard J. Schain, M.D.
- **Resistant Rickets—Refractory Rickets, Renal Tubular Hypophosphatemic Rickets,** by Francis Scott Smyth, M.D.
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Special Issue

Treatment of the Patient with Multiple Injuries

From The St. Paul–Ramsey Hospital

Introduction

Statistics relating to morbidity and mortality from injuries in this country serve to emphasize the magnitude of the problem which trauma presents. In our industrialized urban society, with an increase in the number of motor vehicles each year, there is every reason to believe that the number of injuries will increase rather than decrease. Since the traumatic injury has come to occupy this major position as a cause of disability and death, an issue of The Journal-Lancet devoted to a discussion of the management of the patient with multiple injuries seemed appropriate. The choice of the multiple injury syndrome as the focal point for discussion was made for very practical reasons. Injury of a single organ or part of the body is usually recognized and treated without delay. On the other hand, victims of major accidents may suffer damage to multiple organs and systems. If all significant derangements are to be recognized, a method for determining the full extent of injury and for establishing priorities for treatment is absolutely essential.

Members of the staff of the St. Paul–Ramsey (Ancker) Hospital who have contributed to this issue base their conclusions and recommendations on a large experience with management of traumatic injuries, since the hospital has for many years served as the principal emergency facility for St. Paul and Ramsey County, Minnesota. The diagnostic and therapeutic techniques discussed herein have proved to be simple, workable, and lifesaving.

JOHN F. PERRY, JR., M.D., PH.D.
Guest Editor

The Evaluation and Initial Treatment of the Accident Victim

ROBERT A. VAN TYN, M.D.
St. Paul

BETWEEN 40,000 and 50,000 patients are treated yearly in the emergency room of the St. Paul–Ramsey County Hospital. Approximately 10% of this number are involved in accidents, and less than half of these have serious injuries. Small as their number is compared with the total number of patients, their treatment is time consuming, involves many persons, and taxes the skill and diagnostic acumen of medical personnel to the utmost. Therefore, treatment of the seriously injured patient is considered of prime importance and the main "raison d'être" for the emergency room.

In this hospital, the entrances for ambulatory patients and the ambulance are separated and located at opposite ends of the emergency room. Facilities for the receiving and treatment of the trauma patient consist of a fracture room, a minor surgery room, a gynecological examination room, and two large "accident" rooms. The latter are equipped with suction, oxygen, an anesthesia apparatus, a cardiac pacemaker, monitor and defibrillatory system, and the necessary material and packs to perform cutdowns, thoracentesis, closed-chest drainage, peritoneal lavage, tracheotomy, and emergency laparotomy and thoracotomy.

On arrival, an immediate evaluation of the victim's circulatory and respiratory functions is made by palpating the femoral artery pulse and observing respiration, color, and behavior.

Resuscitation procedures consist of closed-chest cardiac compression and positive pressure ventilation. It is important to insure initial oxygenation of the patient through immediate mouth-to-mouth breathing or the use of a mask and bellows apparatus before attempting endotracheal intubation. Too often expert intubation is not immediately available, and the time spent in attempting to intubate the patient, added to the period of respiratory insufficiency preceding the patient's arrival results in irreversible brain damage due to cerebral hypoxia. If no immediate respiratory or circulatory emergency exists, examination proceeds as outlined in this article.

THE CONSCIOUS ACCIDENT VICTIM

Since the assessment of the type and extent of injuries by nonmedical and paramedical personnel often is inaccurate, it is of great importance to evaluate the conscious accident victim as soon as he arrives and *before* he is transferred from stretcher to emergency room cart. This can be done quickly by noting appearance and behavior of the victim, obvious deformities, and presence of hemorrhage and by asking the patient where he hurts, specifically, questioning him about pain in the back or neck. A brief palpation along the cervical, thoracic, and lumbar spine to elicit tenderness is carried out. The patient is asked to move his feet and hands. Since some spinal lesions can produce a rapidly progressing paralysis, it is extremely important that the presence or absence of paresis or paralysis is noted at the earliest possible moment.

The transfer of a seriously injured patient — especially the patient with multiple fractures or spinal injury — from stretcher to cart requires great care and adequate help. It is our experience that the extent of a victim's injuries often is underestimated by paramedical personnel. On the other hand, when serious injuries are obvious, the tendency exists to act hastily and without proper care. It is the attending physician's duty to prevent this by adequate instruction of personnel, careful evaluation of the accident victim, and proper direction of transfer procedures.

THE UNCONSCIOUS VICTIM

It is assumed that the unconscious accident victim has a spinal injury until proved otherwise. Therefore, resuscitation procedures, when neces-

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ROBERT A. VAN TYN *is director of emergency and receiving room, St. Paul–Ramsey Hospital, St. Paul.*

sary, are started while the patient is still on the ambulance stretcher. He is not transferred to the emergency cart until an adequate number of personnel is available to insure proper transfer. The cervical spine is immobilized manually during transfer and with sandbags on each side of the head thereafter.

All accident victims are placed on a padded plywood litter.[1] Ideally, the patient should be placed on a similar litter at the site of the accident and should stay on it through the evaluation and early treatment period or until his condition permits transfer to a hospital bed. Besides preventing further injury through obviating repeated transfers, it provides the necessary rigidity for the protection of spinal and pelvic fractures and the application of closed-chest cardiac resuscitation. It has proved especially advantageous during diagnostic X-ray procedures.

Further examination of the fully undressed patient is performed systematically with special attention to the head, chest, and abdomen. Pupillary size and reaction are noted. Scalp lacerations are explored with the sterile, gloved hand for evidence of skull fractures. The nose, ears, and throat are checked for bleeding. If bleeding from the external auditory canal is found, no attempt at otoscopy is made but the ear is immediately covered with a sterile dressing.

The chest is observed and palpated for evidence of paradoxical respiratory movement, rib fractures, and subcutaneous emphysema. Percussion and auscultation will reveal hyperresonance or dullness and presence and character of breath sounds. Uncontrollable behavior and panic without obvious cyanosis is often a sign of "air hunger" caused by pneumothorax. Because the severely injured patient frequently cannot be moved from a supine position, auscultation of the posterior chest often is overlooked and a hemothorax is not detected. The bell of a stethoscope can be easily pushed under a patient's back without disturbing his position. If a pneumothorax is suspected, a diagnostic thoracentesis is performed with a 20-cc. syringe, a 3-way stopcock, and a long, 15-gauge needle. The chest is entered in the midclavicular line in the second intercostal space. Free air is removed as much as possible. If a hemothorax is suspected, the same procedure is carried out in the posterior axillary line in the seventh or eighth intercostal space. If a significant amount of blood is aspirated, a large bore chest catheter is inserted in the same site and connected to a water seal suction apparatus.

Penetrating chest wounds are immediately covered with sterile vaseline gauze and a large sterile occlusive dressing.

The abdomen is examined for signs of trauma, distension, and tenderness. Peritoneal lavage, as described elsewhere in this issue, is performed in the emergency room whenever there is suspicion of intra-abdominal bleeding. Upper quadrant tenderness, fractured ribs overlying the spleen or liver, and unexplained hypotension are among the indications for this procedure.

PRELIMINARY TREATMENT

Since many accident victims have lost or are losing blood through external or internal hemorrhage or both, it is of the utmost importance to prevent, recognize, and treat hypovolemic shock. After removal of often inexpertly applied, improvised tourniquets, external hemorrhage is controlled by large pressure dressings and, where possible, elevation. An estimate of blood loss is made by questioning the patient and the ambulance attendants. Although obvious major hemorrhage usually is readily diagnosed, there are some instances where blood loss commonly is underestimated. In our experience, these include:

Scalp lacerations. Especially considered here are frontoposterior lacerations of the temporal and parietal region, where major blood loss has occurred before the victim arrives at the hospital and further blood loss is masked by large bulky dressings.

Multiple fractures. Interstitial bleeding, especially in the case of fractured femurs, can attain life-threatening proportions.

Pelvic fractures. Retroperitoneal bleeding often causes major blood loss without external evidence until the patient's blood pressure drops suddenly.

The unconscious patient with a severe head injury. A fall in blood pressure in such a patient is often erroneously attributed to his brain injury. Careful examination for causes of blood loss must be made and the hypovolemia treated.

The elderly patient. Blood loss, although not major in absolute proportion, may prove catastrophic because of primary decreased blood volume, previously existing hypertension, or cerebral and coronary arteriosclerosis. Extreme vigilance is mandatory in this type of patient.

In these cases and all other accident victims where more than minor blood loss is suspected, a 14-gauge Angiocath is inserted in an arm vein and Ringer's lactate infusion is started.

If major blood loss is suspected or hypovolemic shock threatens, whole blood transfusions are given immediately. It has been our practice to use uncross-matched O-negative blood until typed and cross-matched blood is available. Experienced personnel should maintain close surveillance of the patient who has suffered major hemorrhage or may yet lose a significant amount of blood. Frequent observation of vital signs should be carried out.

It is sometimes wrongly assumed by medical personnel that an accident victim with a low blood pressure but who is mentally alert is not in hypovolemic shock. Adequate instruction will prevent this mistake.

The severely burned patient is received and treated with sterile precautions. Personnel wear masks, gowns, and sterile gloves. The patient is wrapped in sterile sheets and immediately transferred to the burn unit.

Fractured extremities are immobilized whenever possible with "cotton casts." A 1½- to 2½-in. layer of cotton batting is wrapped around the injured limb following the same principles for application of a plaster cast. Two layers of wide elastic bandages are then tightly wound over the cotton. Femoral fractures are immobilized with a Thomas splint and adhesive-strip skin traction. Hip fractures are immobilized with sandbags along the leg.

Wringer and crushing injuries of the extremities often are accompanied by severe edema. In treating these, a large padded pressure dressing in the manner of a cotton cast is applied and the limb is elevated immediately after the victim's arrival.

Tracheotomies are routinely performed in the emergency room on patients with severe chest injuries, patients who are bleeding in the upper respiratory tract, unconscious patients with severe head injuries, and patients with third degree burns of the face and neck.

An indwelling Foley catheter is routinely inserted in the following cases: [1] to diagnose possible urinary tract injury in pelvic fractures, [2] to provide an immediate means of assessing the urinary output of hypovolemic patients as well as all unconscious patients, and [3] to prevent injury to the bladder when peritoneal lavage is planned.

DIAGNOSTIC PROCEDURES

Diagnostic procedures are kept to a minimum. X-rays are, in most instances, of secondary importance. If X-rays are mandatory for the diagnosis and treatment of the critically injured patient, they are taken in the emergency room with a portable X-ray apparatus. Since the quality of X-rays taken with regular X-ray equipment is superior and the radiology department in our hospital is adjacent to the emergency room, X-rays usually are taken there if the patient's vital signs are stable.

A supine chest X-ray frequently fails to demonstrate a significant hemothorax or pneumothorax, or both. In case of a chest injury, therefore, an upright or, if this is impossible, a lateral decubitus chest film (with the injured side up) must be obtained. Cervical spine, skull, and pelvic X-rays are routinely taken on all unconscious accident victims. It is advisable to take skull X-rays on *all* unconscious patients since, in these cases, trauma sometimes is not known or is overlooked.

Because traffic accidents often are directly or indirectly associated with alcoholic intoxication and the victim may have abdominal or head injuries, vomiting is a frequent occurrence. Special attention should be paid at all times to the prevention of aspiration. Close observation of the patient with immediate turning of the head and body to the side and suctioning of the mouth and nose, when possible, are necessary. We routinely empty the stomach through nasogastric suction with a 9-hole No. 14 Wangensteen tube in these cases and when gastric dilatation is evident through percussion or X-ray examination.

The seriously injured patient is routinely treated in the emergency room until his vital signs are stable and no immediate danger of circulatory or respiratory distress exists. The patient then is transferred to the intensive care unit. Keeping patients under close observation by professional personnel during transfer is of vital importance. It is a tragic occurrence to lose a critically injured patient, who has been successfully treated initially, through untimely or unsupervised transfer.

In spite of the general excellence of available first aid courses, it is our experience that the first aid of the unconscious and severely injured patient presents a great problem to police, rescue, ambulance, and other personnel responsible for the first aid treatment of the accident victim. Any physician involved in emergency care and treatment would do well to take an active part in the instruction of first aid personnel.

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The Emergency Care of Cerebral Injuries

WALLACE P. RITCHIE, M.D.
St. Paul, Minnesota

In a review of the autopsy findings in 127 patients involved in fatal traffic accidents, Perry and McClellan[1] found that head injury was the primary cause of death in approximately 47% of the patients. Slatis,[2] in analyzing 349 medical-legal autopsies, reported deaths from head injuries to be as high as 56%.

The care of the acutely injured patient has developed to such an extent that the patient who arrives at the hospital has a far better chance of surviving than he did ten years ago. Numerous factors contribute to this lowered mortality. In the first place, abdominal injuries are more easily recognized—even in the unconscious patient—due to peritoneal lavage introduced by Root.[3] Advances made in the care of chest injuries are particularly striking, and supportive care of the patient is better understood.

The patient with a head injury has a better chance of surviving, not only because of these changes but also because of a changing concept regarding these injuries. Until now, it was accepted that the cause of a disastrous symptom of head injuries, that is, unconsciousness and vasomotor disturbances, was due primarily to dissolution and disorganization of the cerebral hemisphere. Whereas the primary injury may well be in the hemispheres, the major cause of deterioration is a secondary effect on the subcortical areas. This is primarily in the brainstem, with its important midline structure, the reticular substance. The brainstem, for our purposes, includes the hypothalamus, midbrain, pons, and medulla. It is packed with neuron centers and relay stations with fibrous tracts, which serve every known vital function. Furthermore, in the center, extending from the medulla to the hypothalamus, is a neuronal core which is loosely connected anatomically by long fibrous pathways and receives sensory input from all sensory systems.

This system acts closely with the thalamus and cortex to maintain the "awake" state. It is the reticular activating system. It lies on the bony floor of the skull and is subject to pressure from above as well as to twist and torsions. It is, as one might say, the final common pathway of the effects of a head injury. The brainstem may be thrown up against the clivus, rendering the patient immediately unconscious. If the midbrain is not directly injured by this source, the patient will not be unconscious for any length of time. But if edema or hemorrhage intervenes, pressure on the brainstem can occur and the patient will gradually lapse into unconsciousness.

Other physiological changes are noteworthy. It has been demonstrated that, following a head injury, vasospasm and subsequent slowing of the bloodstream occur. This requires adequate oxygenation. There is liberation of acetylcholine, which can act as a depressant of the activating system. Some schools give large doses of atropine to combat this. Foltz[4] has reported some interesting observations in experimental concussion, one of which is respiratory paralysis. As a rule, a physician is not present at the time of the accident. Therefore, valuable time may be lost in maintaining an adequate airway and even in giving artificial respiration.

EVALUATION

In evaluating a head injury, one must take into consideration the separate entities which can occur.

Scalp lacerations. Although self-evident, a scalp laceration should never be sutured without first ascertaining whether there is a depressed fracture beneath it. Shock from loss of blood is rare, and only 3% of those with head injuries are in surgical shock. If this state is present and there is insufficient reason for shock to take place from the laceration, one must always consider injury to other organs, such as the spleen or liver.

Fractures. Skull fractures may be linear, depressed, or basilar. Linear fractures themselves are of little significance. However, if they cross branches of the middle meningeal artery or if they cross the longitudinal or saggital sinuses, one must be doubly alert for the development of an extradural hematoma. Depressed skull fractures

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WALLACE P. RITCHIE *is clinical professor of Neurosurgery, University of Minnesota, and Chief of Neurosurgical Service, St. Paul–Ramsey Hospital.*

should be elevated when convenient. The significance of basilar fractures, even if not seen by X-rays, is the danger of meningitis developing. Every patient with bleeding from the ear or nose should be placed on antibiotics. X-rays of the skull should be taken on admission, if possible.

Intracranial injuries. Four entities which occur intracranially must be evaluated. These are [1] concussion, [2] contusion or laceration of the brain, [3] edema, and [4] subdural, extradural, or intracerebral hemorrhage.

Pure concussion is reversible. The numerous definitions of concussion are usually related to the state of unconsciousness. But generally speaking, a person who recovers from the state of unconsciousness without any residual pathological signs is said to have had a concussion. It is always associated with loss of consciousness and, therefore, is accompanied by a varying degree of retrograde anemia.

Contusion and laceration of the brain and intracranial hemorrhage are closely allied, and the diagnosis of one or the other, or both, is difficult. However, the one important aspect to determine is whether or not the patient has or is developing a surgical hematoma. A surgical hematoma will cause increased intracranial pressure.

The determination of increased intracranial hemorrhage can be made by numerous methods: checking the vital signs, spinal puncture, changing neurological signs, funduscopic examination, and the patient's response.

Of all the tests available, the response of the patient is by far the most important. The state of consciousness should be checked frequently, for a deepening state of unconsciousness means that the brainstem is being compromised and this may be due to hemorrhage or edema. When first attending the patient, it is wise to determine his state of consciousness by applying a noxious stimulus to an area just posterior to the parotid gland at the angle of the jaw. On first examination, he may grimace with both sides of his face and throw up both arms. During a second application, it may take more pressure to awaken him and he may grimace with only one side of his face and raise one arm. Thus, with a simple maneuver we know that he is more stuporous and has a hemiparesis.

An evaluation of the pupils is essential because a dilating, poorly reacting pupil usually means pressure is developing on the same side.

The vital signs often will give an indication of increased intracranial pressure, particularly in the rapidly developing extradural hematoma. A decrease in pulse rate and an increase in diastolic pressure are indications of increased intracranial pressure.

As a rule, spinal puncture is not advocated in acute head injuries.

Special X-rays, such as angiography, are helpful, but usually a diagnosis of the intracranial hemorrhage can be made without them.

TREATMENT

The emergency care of head injuries falls into two categories—surgical and supportive.

Surgical. Trephination, evacuation of the hemorrhage, and control of bleeding comprise the basic surgical treatment. If a fracture line crosses a branch of the middle meningeal artery, the first trephine should be over that point. If a subdural hematoma is found, three trephines are indicated to permit thorough washing. A fourth trephine should be done on the opposite side.

Supportive. The supportive care is another matter. In the first place, an adequate airway is essential. Foltz[1] has shown that, at the time of injury, there is respiratory paralysis, and every effort should be made to combat this temporary paralysis.

Early tracheotomy is indicated in all patients with difficulty in obtaining air. One must not, however, perform unnecessary tracheotomies.

The electrolyte balance should be carefully watched. Ordinarily 1,000 cc. of fluid is sufficient for the first twenty-four hours, but thereafter adequate fluid intake is essential. At least 2,000 cc. should be given every twenty-four hours. If the patient is unable to take nourishment by mouth for six days, gastric feedings should be instituted, taking care that the patient does not aspirate the feedings.

Some degree of edema accompanies most head injuries. Various methods have been used to control this, but at present the most efficient method is use of 5 to 10 mg. of dexamethasone (Decadron®) every six to eight hours. The effect of this is not well understood, but there is little question that edema of the brain is significantly lessened by its use.

The one principle by which all head injuries should be treated is that a deepening state of unconsciousness must always be considered to be due to hemorrhage until proved otherwise.

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Eye Injuries

ROBERT HUGH MONAHAN, M.D.
CHARLOTTE WEEKS HILL, M.D.

St. Paul, Minnesota

IT HAS BEEN ESTIMATED by the National Society for the Prevention of Blindness that in industry alone over 300,000 eye injuries occur yearly. Of these, 100 lose all eyesight in both eyes. The early recognition of eye injuries is of utmost importance. The consequent measures taken immediately to treat the injury or to prevent further injury often are in the sphere of the family doctor and the general surgeon. The eye problem may be a minor factor in an extensively injured patient, or with the patient unconscious and the eyes closed, a major ocular injury may easily be overlooked if the eyes are not examined.

The importance of an adequate history regarding the injury cannot be overemphasized, as it may prevent many medicolegal problems; it may guide the physician in the type of injury to be found and may allow a more reliable prognosis. The adage stating the necessity of "who, what, where, when, how, and why" on the record of the first visit is of invaluable help in future reporting and testimony.

It is not usually necessary to give complete immediate care to the injured eye. On the contrary, it is often better to protect the eye against further injury and await the arrival of specialist care. The one ophthalmologic emergency demanding immediate definitive care is the treatment of the chemically burned eye. Irrigation with copious amounts of the most easily available innocuous fluid (usually tap water) for ten minutes, while forcibly keeping the eyes open, should be immediately performed. This may be done, in industry, at the site of the injury and by the patient's fellow workers before transportation to the medical station. If possible, attention should be given to the skin of the lids and to the fornices in order to remove all of the fluid or precipitated chemical present. This is most important in cases of alkali and caustic burns. Acid burns tend to cause precipitation with the cellular proteins and thus form a protective layer against further penetration. On the contrary, alkali substances tend to continue to penetrate. This is the principal ocular injury that demands immediate definitive care. Irrigation should be performed before calling the doctor, before the history is taken in detail, and before the vision is checked or recorded. Searching for a specific neutralizing fluid is unnecessary and is a waste of valuable time.

The vision should be tested before treatment is instituted, with the exceptions of the chemically burned eye, the unconscious patient, or the individual in such extremely grave generalized condition that lifesaving measures must be taken first. The Snellen chart should be used preferably. If the vision is so blurred that the largest letter cannot be perceived, then the patient is asked the number of fingers that the examiner holds up. If this, too, cannot be perceived, then the presence of hand motion is tested and recorded. If the patient is unable to see when the hand moves and when it is still, then the ability to perceive light is tested by using a flashlight, preferably one with a noiseless switch. If Snellen chart is not available, the ability to read may be checked and recorded as "perceived newspaper story print, headlines with letters ½ in. high, typewritten size print," or other appropriate phrase.

After the history and visual acuity are recorded, the evaluation of the condition of the eye may indicate the need for an eye specialist's care. While awaiting the arrival of such care, during transportation of the patient, or while other bodily injuries are being corrected, the proper protection of the injured eye may be as important as anything the ophthalmologist can do later. A protective device over the injured eye will help prevent the patient or his family from examining

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ROBERT HUGH MONAHAN *is clinical associate professor, University of Minnesota, Minneapolis, and on the staff of St. Paul–Ramsey Hospital, St. Paul, and* CHARLOTTE WEEKS HILL *is clinical instructor, University of Minnesota, Minneapolis, and on the staff of St. Paul–Ramsey Hospital, St. Paul.*

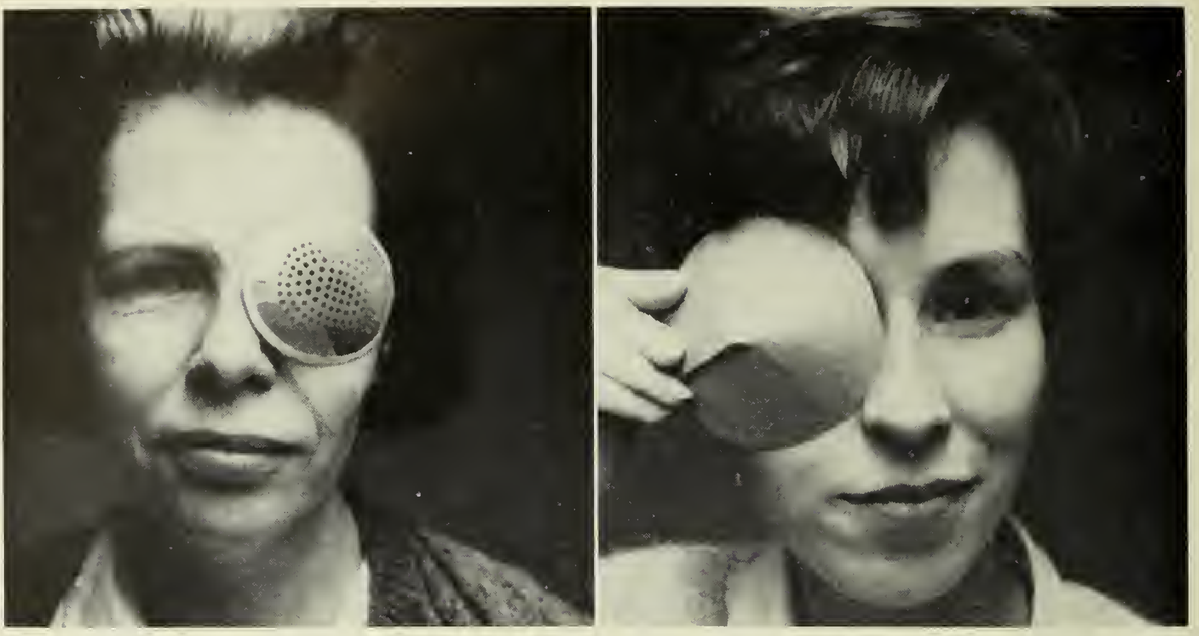

Fig. 1. Protection of the eye may be achieved [A] by use of perforated metal shield taped in place or [B] by cutting out a circular piece of cardboard, cutting one radius, folding the cardboard on itself, and taping it in place over the injured eye.

or attempting to help and will protect the eye while other injuries are being treated. In addition, a simple eye pad over the intact eye will help prevent further injury by blocking some of the bilaterally innervated mechanisms of the eyes and by helping the patient to lie down quietly. A perforated metal shield or an improvised shield cut from cardboard will similarly help protect the perforated eye. The patient should be supine without his head turning from side to side. Medications for pain and the use of sedatives are recommended whenever indicated. It is wise to take the precaution of giving the patient nothing by mouth until the ophthalmologist arrives.

Another measure that may need to be taken before specialist care is available is the placement of foreign particles removed from a perforated or partially penetrated site of the eye directly onto a blood agar plate. Because of the difficulty in achieving adequate concentrations of antimicrobial medications inside of the eye in cases of intraocular infections, the information obtained from cultures and sensitivities performed on these foreign substances may be all-important in the management of the injured eye. This situation is often encountered by the ear, nose, and throat specialist or the general surgeon when repairing massive facial injuries and lacerations. If possible, it is preferable that such foreign bodies be left in place until the ophthalmologist has an opportunity to evaluate the situation. However, this cannot always be done.

The complications of eye injuries are numerous and include cosmetic deformities, excessive tearing, cataracts, uveitis, glaucoma, retinal detachments, macular tears and hemorrhages, rupture of the choroid, and loss of the eye itself, either early or many years later. The nonopthalmologist should be cognizant of the extent of the injury presented to him, the methods of treatment, and the consequences and possible complications that the patient may have to face.

BLUNT TRAUMA

Ecchymosis of the eyelids (the common "black eye") is often a minor injury and requires little, if any, treatment. However, it may be associated with more extensive damage. Bleeding from the ears in association with a black and blue eye may indicate the presence of a skull fracture. Fracture of the bony rim of the orbit may be present with or without crepitus of the orbital tissues. Limited ocular movement with diplopia may be due to a blowout fracture of the orbital floor with prolapse of the orbital contents into the bony defect. If the eye has limited movement in the down and in position, the trochlea of the superior oblique muscle may have been torn off its attachment to the superior orbital bone.

When the globe is injured by blunt trauma, it is best to transport the patient by litter or by ambulance. Injuries to the globe from blunt trauma can affect any part of the eye. For example, a simple conjunctival hemorrhage may be present and represent a minor injury. Conversely, it may mask a deeper rupture of the sclera or, if massive, may indicate a posterior rupture of the globe, a fracture of the bony orbit, or a fracture of the base of the skull. An abnormally deep anterior chamber may be present with or without a posterior dislocation of the lens or a subluxation of the lens. An anteriorly dislocated lens may cause an intractable acute glaucoma. Traumatic cataracts may form very rapidly within a matter of hours, or months may be required before their presence can be detected.

Intraocular lacerations and tears may include all parts of the uveal tract. If the choroid is ruptured, the macula is commonly involved and a severe permanent visual loss results. Anteriorly, an intraocular hemorrhage (hyphema) may be present and is always a sign of internal injury. The patient should be put on bed rest and bilateral patches should be used. This type of hemorrhage usually clears on such treatment, but occasionally a secondary hemorrhage occurs and, with it, secondary glaucoma and permanent blood staining of the cornea. A paracentesis often should be performed at the onset of such a secondary glaucoma.

Retinal detachment, rupture of the optic nerve, macular edema, hemorrhages in the posterior segment, and paralysis of the sphincter muscle of the iris may also occur. This latter effect of trauma may show itself by a fixed, semidilated pupil that is round or irregular in shape or eccentric in position.

LACERATIONS

When a laceration of the skin of the eyelid is involved, it too often is through-and-through and extends into the globe underneath. However, on cursory examination, it may appear to be superficial and limited to the skin of the eyelid. Because of this, the globe should be fully examined. This is especially true when the injurious agent is a high-speed missile or a sharp object. When the lid margins are involved, the accurate approximation of the tissues is important to prevent cosmetic and functional defects. Canalicular involvement presents a difficult problem even to the most experienced ophthalmic surgeon. Permanent damage to the inferior canaliculus may cause a serious physical handicap. A silver wire, polyethylene tube, or silk suture should be placed through the punctum, through the cut ends of the canaliculus, and into the lacrimal sac and brought out through the skin overlying the sac. This should be left in place for many weeks in hope that the lumen will remain patent.

When there is a loss of substance of the lids, corneal exposure may result from poor closure. Suturing both of the eyelids shut temporarily with extensive skin grafting at a later date may be required. Debridement may be necessary, but it is best not to remove skin tags from eyelid lacerations in an effort to create a sharper line of suturing. The blood supply to the eyelids is excellent, and contrary to what may be recommended in other parts of the body, all tissue should be preserved if it is viable. Scarring is at a minimum in the eyelid skin.

Many times, the evaluation of the condition of the levator muscle, lid margin approximation, and the canaliculi requires the detailed anatomic knowledge of the ophthalmic surgeon.

Lacerations of the conjunctiva, if small, will often heal well without surgical closure. If larger, a running 6-0 plain catgut suture may be put in place under local anesthesia. Because of the threat to vision and the medicolegal implications, lacerations of the sclera and cornea are best left up to the care of those skilled in this type of surgery.

ABRASIONS AND ULCERATIONS

The patient often will complain of a foreign body sensation and report his symptoms as occurring at a specific time at work or at home. One can be fooled by this, for examination of the eye may show a dendritic ulcer, which is pathognomonic of herpes simplex of the cornea. This corneal virus ulcer may also be found as a result of a previous foreign body or traumatic abrasion of the cornea. The possibility of the presence of this virus infection must be kept in mind because the use of topical steroids is strictly contraindicated in its presence.

Corneal abrasions, caused by fingernails and shrubbery, are especially painful. One is tempted to relieve the suffering with the repeated use of topical anesthetics. However, if it is borne in mind that corneal epithelial healing will be long delayed because of the absence of mitoses when topical anesthetics are used, it is easier to explain to the patient why other measures are being taken. It is wise to use topical anesthetics at the time of examination in order to obtain a more complete and satisfactory examination with a patient who is able to cooperate, but no anesthetic drops should be given to the patient for self-application. The lesion may be outlined by the use of fluorescein which will stain an area denuded of epithelium a bright green. It is recommended that the sterile fluor-

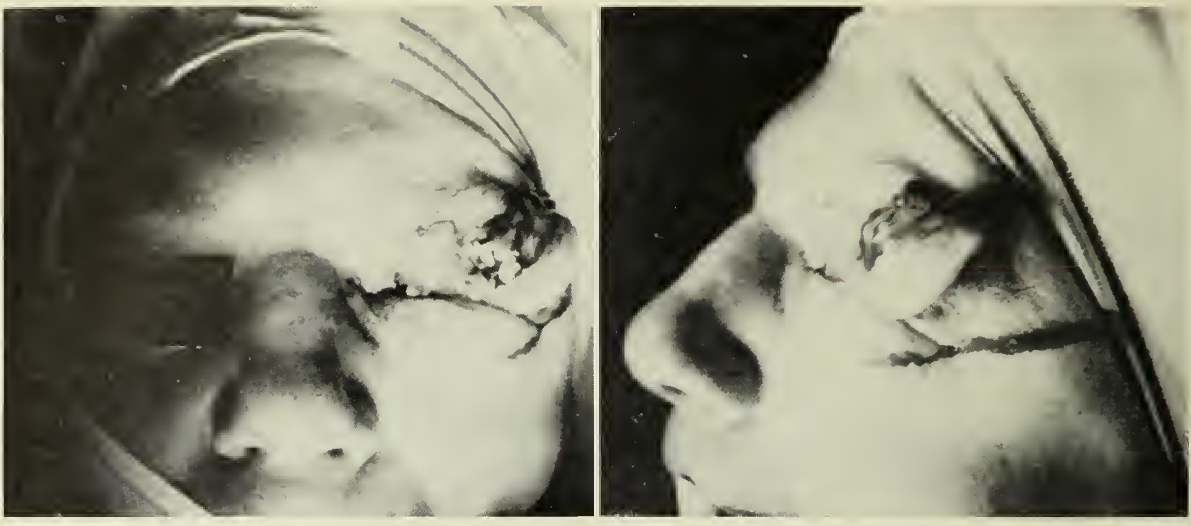

Fig. 2. Massive eye injury caused by a hook or a conveyor belt. [A] Front view: the entire upper eyelid is avulsed and lies temporally with its conjunctival surface exposed. The lateral rectus and superior oblique muscles were severed and the eye is fixed in the in and down position. The orbit is exposed above the globe and inferior to the cut surface of the upper lid. [B] Side view of same patient

escein strips be used, moistened with sterile normal saline or by the patient's copious tears. These strips are easily kept on examining trays and in medical bags and may be used if unopened and uncontaminated even after many years. Fluorescein in fluid form is an excellent medium for the growth and multiplication of many bacteria, especially Pseudomonas aeruginosa. This organism has been known to cause a perforation of cornea within twenty-four hours. These facts account for the popularity of the fluorescein strips.

The corneal abrasion is best treated by a firm pressure dressing over the eye to prevent mechanical removal of the healing epithelium by the action of the eyelids. Systemic medications for pain may be used if needed. A topical antimicrobial agent is to be recommended and may be instilled before the eye pad is put in place. The pad is then left in place twelve to twenty-four hours before the eye is reexamined.

CHEMICAL AND PHYSICAL BURNS

Physical burns are treated much the same as chemical burns except that copious irrigation is not needed. The use of antimicrobial medications is advised in both cases. Later treatment may require extensive grafting of the skin, the cornea, or areas of sclera. Physical burns are most commonly seen as welding burns, overexposure to sunlamp light rays, and electric burns. These injuries consist of areas of epithelial loss with consequent exposure of the corneal nerve endings giving considerable discomfort to the patient. Pressure dressings are used after instillation of topical antimicrobial agents, and the eye should be examined again twenty-four hours later.

FOREIGN BODIES

Superficial foreign bodies constitute the most common form of ocular injury. Those on the cornea that may be irrigated away with a forceful stream of sterile normal saline rarely cause a complication. The foreign body on the inside of the upper lid can be detected only by everting the lid. The cornea often will show multiple abrasions from the action of the lid. The foreign body may be removed with a sterile cotton-tip applicator after the instillation of a topical anesthetic. An antimicrobial medication should be used, and the eye may require a pressure dressing for twenty-four hours because of the corneal abrasions.

Corneal foreign bodies that cannot be removed by irrigation and that lie off the pupillary zone may be removed by use of a spud or, if that is not available, by using a hypodermic needle on a tuberculin syringe. Preferably, the foreign body should be lifted out with a single action to prevent adding further trauma. A cotton-tip applicator should not be used on the cornea because it inflicts a much wider area of ulceration than that already caused by the presence of the foreign body. These foreign bodies should be removed when found and not "left in place for a day or two to see if they will work their way out." The use of topical anesthetics, a good light source, some form of magnification, and a good instrument will keep the trauma to a minimum and give the least amount of scar tissue.

The corneal foreign body in the pupillary zone is best removed by an ophthalmologist with the aid of a slit lamp microscope, as it is important to have as small an area of scarring as possible. Again, topical antimicrobial medication and a pressure dressing are advised for a twenty-four-hour period, and the eye should be reexamined at that time.

Penetrating foreign bodies that are retained in the eye are capable of causing complete loss of function of the eye with deformity and pain. Those protruding from the site of perforation are rather easily detected. However, foreign bodies that penetrate the outer coats of the eye with considerable speed may leave a very small point of perforation that seals quickly and the retention of the particle may not be known for weeks. The history is of special importance in such a case, for then the eye is examined in detail with full dilatation. If the foreign body is metallic, radiologic examination will help to detect its presence and can aid in localization. If the particle is nonmagnetic, the prognosis is poor for retaining the eye. If the injury is so severe that the globe cannot be sutured to maintain its form, enucleation is indicated. The perforated eye that shows prolapse of uveal tissue is usually treated with excision of the prolapsed tissue and closure of the outer layer (cornea or sclera). The next several days will show whether enucleation of the eye is indicated in order to prevent sympathetic ophthalmia of the fellow eye.

CYCLOPLEGICS

Atropine is indicated in the treatment of secondary iridocyclitis following trauma to the eye. When used unnecessarily, it may be incapacitating to the patient for seven to fourteen days. The danger of precipitating an acute glaucoma in the injured eye must also be borne in mind. Two percent homatropine and 0.2% scopolamine are shorter acting than atropine (a matter of hours) and often give the eye considerable comfort and they are frequently used after a foreign body is removed, before the dressing is applied.

ANESTHETICS

The use of these medications other than to facilitate the examination or during removal of a foreign body has been mentioned and condemned. Tetracaine hydrochloride (Pontocaine®), benoxinate hydrochloride (Dorsacaine®), or proparacaine hydrochloride (Ophthcaine®) are commonly used. It might be noted that a red inflamed eye with conjunctival or corneal edema will require more anesthetic than a quiet white eye.

ANTIMICROBIALS

The sulfonamides used topically on the eye have about equal effectivity. Sulfisoxazole diethanolamine (Gantrisin®) and sulfacetamide sodium are both widely employed. When antibiotics are used, it is important to attempt to choose those whose use systemically is limited. Polymyxin B-bacitracin-neomycin (Neosporin®) and polymyxin B-bacitracin (Polysporin®) are commonly used combinations of such medications. They have a broad spectrum, and allergic reactions are rare.

STEROIDS

The development of steroids has been a great advance in ophthalmic therapy, but the complications of their use should be stressed. The incidence of secondary fungal and viral infection can lead to serious consequences, such as the occurrence of herpes simplex with consequent perforation of the cornea. Long-term use of steroids can precipitate secondary cataracts and glaucoma. Most superficially injured eyes do not need these medications. When they are used, the complications must be well known and all available precautions should be used.

SUMMARY

The immediate definitive care of the chemically burned eye is important first aid treatment and should be performed by the person nearest to the injured patient without delay. Other eye injuries can, with the eye protected against further injury, be delayed until the visual acuity is recorded, the history is taken, adequate examination is done, and full facilities for giving definitive care are available.

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The Facial and Laryngeal Injury

JEROME A. HILGER, M.D., DOUGLAS R. KUSSKE, M.D.,
ALBERT HOHMANN, M.D., and BARCLAY M. CRAM, M.D.

St. Paul

THE SKELETAL COMPLEX of the face is formed by the union of 3 unpaired bones with 7 paired bones. Structural weaknesses cross suture lines (Fig. 1). Certain fracture complexes are classic.

The largest of the unpaired bones is the mandible. It supports the lower facial third and articulates with the skull base in the glenoid fossae of the temporal bones. The vomer bone and the ethmoid bone form the bony nasal septum and enclose the nasal vault at the cribriform plate. The lateral aspects of the ethmoid bone are honeycombed pneumatic labyrinths that support the medial aspects of the orbital content bilaterally against their paper-thin bony laminae. Nestled forward between the anterior edge of the ethmoidal labyrinths and the frontal processes of the maxillae are the lacrimal bones. Atop the frontal processes, the pyramid of the central third of the face is closed by the nasal bones as they join on the supportive ridge of the middle or septal plate of the ethmoid. The frontal processes of the maxillae are strong in this support but weaken laterally on the infraorbital margin, where they abut the long, slender, overlapping medial processes of the malar bones. The latter bones, often termed zygomata, are sturdy blocks lying against the lateral superior surface of the maxillae, being as one with them in enclosing those aspects of the maxillary sinuses. The malar bones unite at the upper lateral orbital boundaries with the frontal bones. Strong, arch-like processes extend posteriorly to join with others from the temporal bones to form the malar arches. These arches give firm attachment to the masseter muscles, while beneath them sleave the bellies of the temporal muscles to attach to the coronoid processes of the mandible. Inferiorly, the strength in union of the malar and maxillary bones shades off to the relatively thin canine fossae portion of the maxillae which at the medial rims forms the pyriform aperture of the skeletal nasal opening. Thus, the sturdy alveolar and palatal portions of the maxillary bones hang suspended by the thinner and weaker walls of the pneumatic chambers. Posteriorly, this frailty is buttressed by the pterygoid processes and the vertical shafts of the palatal bones. Somewhat loosely fastened to the nasal aperture of the maxillary sinuses are the inferior conchal bones.

Jutting from the apex of this central facial pyramid in a position of unwarranted challenge is the quadrilateral or septal cartilage capped by the paired upper and lower lateral cartilages. It, together with the vomer bone and the middle plate of the ethmoid, is perched precariously atop the nasal ridge of the palatal and maxillary bones and the anterior nasal spine of the palatal maxillae. And thus is formed the nasal septum—that inquisitive structure so prone to intrusion and trauma.

Hanging from the skull base and the lower mandibular margin are the hyoid bone and the laryngeal complex. Their taut suspension between the mandibular symphysis and the anterior brim of the thoracic inlet is essential in the mechanics of an open airway. While normal tonus is present in the strap and suprahyoid muscles, the laryngeal aperture cannot occlude against the anterior vertebral surface regardless of body position. Since the larynx and the hyoid are protected by retrocession and a high degree of mobility, they are not frequently injured.

IMMEDIATE POSTINJURY CONSIDERATIONS

Fracture of the facial skeletal components may be single and simple or quite complex. In assessing the injury, the whole patient should get primary consideration. The airway is the first vital concern. The unconscious patient with inadequate reflexes will aspirate the blood and secretions pouring backward into his pharynx. A face down position will prevent this to a large degree.

JEROME HILGER, DOUGLAS R. KUSSKE, ALBERT HOHMANN, *and* BARCLAY M. CRAM *are associates in otolaryngology in St. Paul.*

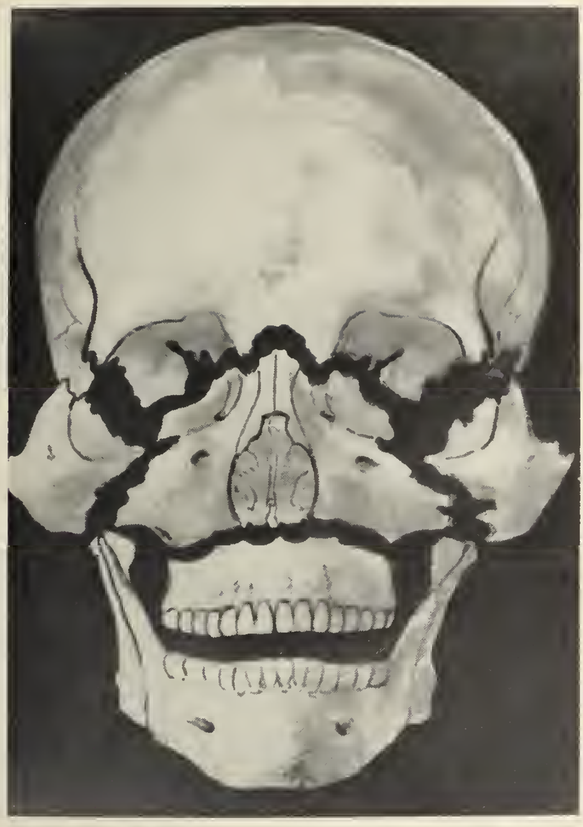


Fig. 1. The skeletal complex of the face is composed of 3 unpaired bones and 7 paired bones. Structural weaknesses cross suture lines

Fracture-recession of the mandible allows the tongue, hyoid, and larynx to drop back and close the laryngopharynx. Traction on the tongue can correct this and can be maintained manually, by a safety pin or by an airway when available. The face down and sideward position helps.

Fracture of the hyoid bone or thyroid and cricoid cartilage, or both, is not relieved by any of the above and requires a prompt tracheotomy if the patient is to survive.

For the severely injured person, the first post-injury week revolves to a great extent around airway considerations. When a state of profound unconsciousness continues, the patient's pulmonary drainage is confounded by the absence of an adequate swallow reflex. This is often compounded by aspiration of nasooral secretions. Partial respiratory obstruction results. Where mandibular and maxillary injury are present, fixation of the bones in firm occlusion must be contemplated. The upper respiratory obstruction of jaw occlusion and nasal airway trauma creates restlessness and anxiety. Sedatives and opiates speed a malicious sequence by diminishing reflexive protections. Airway access for anesthetic procedures is impeded, particularly in multiple-stage repairs. Procedural uncertainty in these circumstances should be resolved in favor of tracheotomy. Pulmonary drainage as well as airway are thus assured. Brain injury, if present, is not compounded by hypoxia. The patient rests well. Anesthetic procedure is no longer a problem.

In ordinary maxillary or central facial third injuries, these considerations do not apply and tracheotomy is not usually necessary.

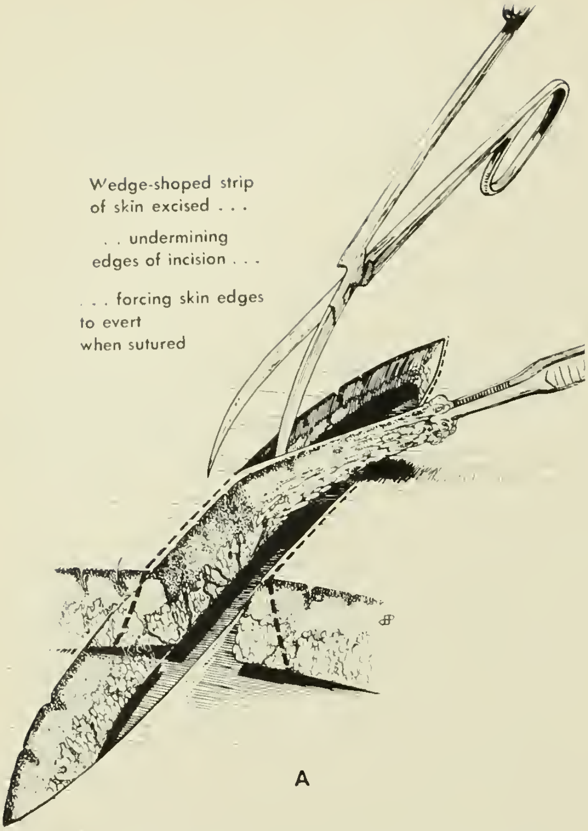
Immediate blood loss from external lacerations and from mucosal surfaces may seem alarming, but it actually is rarely serious. Vessel retraction in the soft tissues of the face is usually prompt and a compression dressing is then adequate.

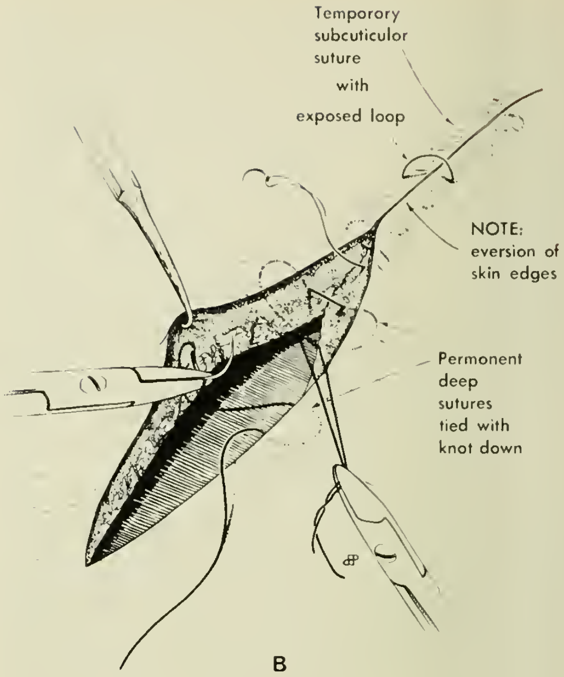
SOFT TISSUE REPAIR

When general circumstances make surgical delay advisable, facial soft tissue injury can be protected with a compression dressing for twenty-four hours. If longer delay is unavoidable, the soft parts can sometimes be cleaned, trimmed, and repaired at bedside with the aid of local anesthesia. Access to the skeletal fragments through the lacerations is frequently important for direct wiring and ideal fixation. It is necessary on occasion to open repaired lacerations for this purpose. The greatest aid to ideal soft tissue approximation is perfect skeletal realignment.

Debridement of facial wounds can be conservative but must be thorough as to depth. All surface tattooing should be removed. Suture materials of 6-0 and 5-0 gauge with comparable needles should not be exceeded. Gentle handling of tissues is mandatory. Magnifying loupes increase the precision of repair (Fig. 2A, B, and C).

Closure must be in layers with no tension exerted at the skin surface. For repair of lacerations into mucosal-lined spaces, thorough mucosal approximation is the primary step. Skin sutures should not be placed wide of the laceration margins. Subcuticular techniques are excellent in soft tissue repair. The outer suture can remain for a week. Adhesive supports can be applied in addition to skin sutures. Edema and serum pooling are prevented by elastic dressings—circumferential are best when possible. Crusting at the repair lines is undesirable and is prevented by moistening the dressings at the incision lines with dilute neomycin solution for the first three days. Thereafter, softening ointment of neomycin and gramacidin, polymixin-type, is desirable. Interrupted sutures must be divided in forty-eight hours and removed in seventy-two hours. Adhesive bridging is applied for support at the time of suture


Wedge-shoped strip of skin excised . . .
. . undermining edges of incision . . .
. . . forcing skin edges to evert when sutured
A


Temporory subcuticulor suture with exposed loop
NOTE: eversion of skin edges
Permonent deep sutures tied with knot down
B

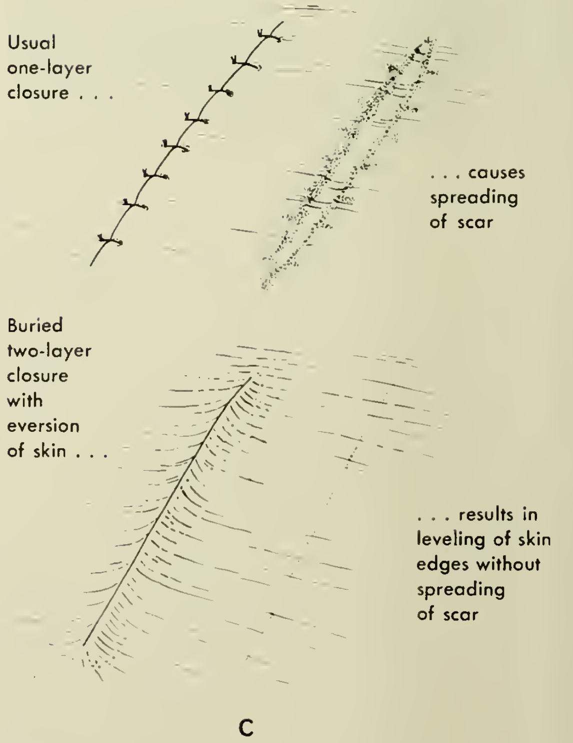

Usual one-layer closure . . .
. . . causes spreading of scar
Buried two-layer closure with eversion of skin . . .
. . . results in leveling of skin edges without spreading of scar
C

Fig. 2A, B, and C. The basic principles of soft tissue repair—careful debridement, closure in layers, fine instrumentation and suture, and loupe magnification

division. Antibiotics and good facial blood supply reduce infection to a minimum as long as debridement is adequate and mucosal surfaces have been properly approximated.

After the primary three weeks' healing is complete, the facial scars should be massaged lightly with bland skin cream for five minutes four times a day to improve mobility and elasticity in the healing scar.

SKELETAL REPAIR

Visual, manual, and X-ray examination will determine the best program for the facial skeleton repair. The objectives are good nasal function, good dental occlusion, normal ocular fusion, and the best cosmetic result obtainable.

The nose. The composite of bones and cartilage collectively termed "the nose" leads all skeletal parts in fracture frequency. The superior one-third to one-half of the projecting portion of the nose is formed by the frontal processes of the maxillae surmounted by the nasal bones, which unite atop the middle ethmoidal plate of the bony septum. This complex may shatter in the manner of an eggshell as a result of central facial third impact (Fig. 3). The characteristic front seat passenger smash into the dashboard produces this injury. The frontal process of the maxilla if sufficiently sturdy may fracture at the infraorbital abutment with the malar bone and impact with the lacrimal bone into the ethmoid labyrinth.

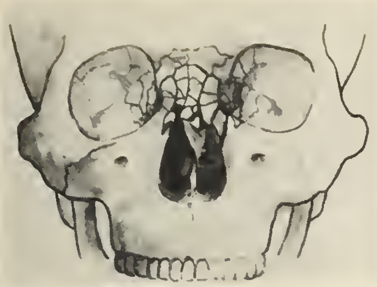


Fig. 3. Comminuted (eggshell) nasoethmoidal fracture

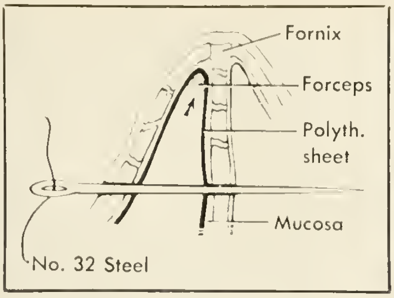


Fig. 4. Method of elevation of comminuted nasomaxillary elements and insertion of wire transfixion at the base

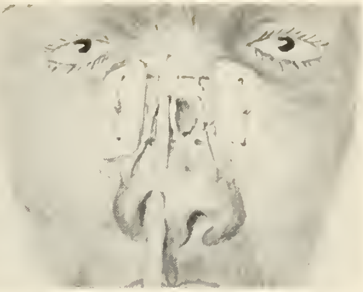


Fig. 5. Completion of wire transfixion techniques for comminuted nasoethmoidal fracture

The usual athletic injury fracture dislocates the nasal bones from on top the frontal processes of the maxillae. The latter may fracture from the main body of the maxillae as well. In either case, the septal plate of the ethmoid is carried in the direction of displacement. This must be reckoned with in the course of reduction.

Injuries of the upper nasal segment are easy to diagnose and delineate by palpation and inspection. X-ray examination is much less informative though perhaps more impressive. Doubt whether fracture has occurred can be resolved by looking and feeling again in a few days when soft tissue swelling has subsided. This delay does not prejudice the final result.

Realignment of these fractures can be accomplished by intranasal and external manipulation and molding. General anesthesia is frequently desirable. Usually, the fragments maintain reposition without splinting. An external molded dressing is sometimes useful to minimize dorsal edema. The latter can result in slippage of fragments. In addition, it can result in undesirable thickening due to organization of transudate. A modest intranasal support of petrolatum gauze strip high in the fornix can be useful to prevent impacted fragments from falling back into the chamber. Intranasal packing stuffed into the nasal space to counter bleeding is a useless and harmful routine measure.

If comminution is extensive and manual elevation of fragments will not maintain position with these simple efforts, direct wiring and pinning are necessary. Two 32-gauge steel wires threaded

Fig. 6. Palpation of the cartilaginous nasal dorsum and caudal end of the septum to identify fracture of the cartilaginous nasal segment

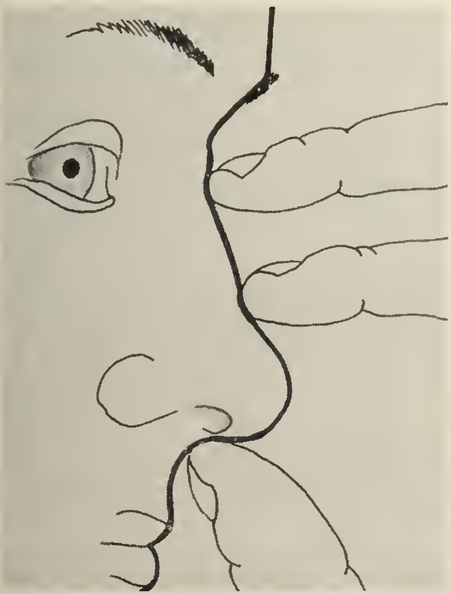
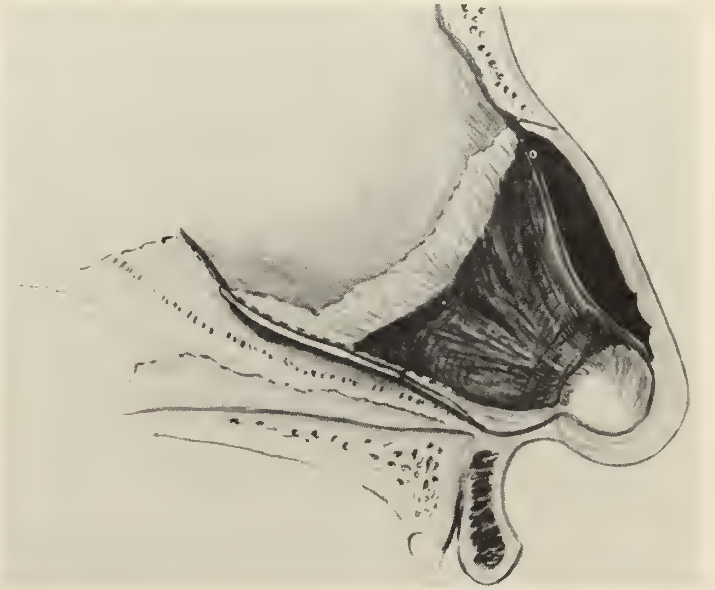


Fig. 7. Dorsal hematoma "soft spot" denoting fracture dislocation of the cartilaginous septum. The mucosa of the intranasal respiratory vault at the upper lateral-septal cartilage juncture is dissected and ballooned downward into the airway.



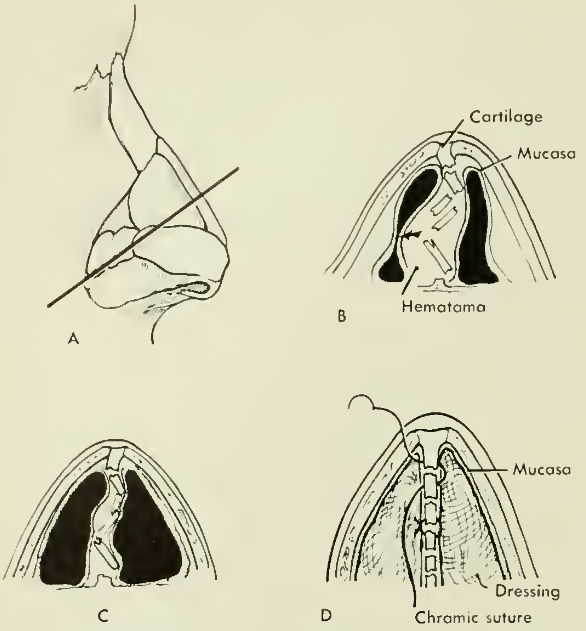


Fig. 8 [A and B] Cross section of comminuted fracture of the nasal septum. [C] Organization in septal disarray with lowering of the respiratory vault. [D] Open reduction, hematoma aspiration, and mattress realignment of the cartilaginous septum

on straight needles are passed through the base of the bony nasal mass (Fig. 4). Comminution makes this maneuver easy or the needle can be drilled through. The wires are threaded through molded lead plates and the latter are snugged to the nasal skeleton to support an agreeable contour (Fig. 5). Incorporation of a sheet of synthetic film draped over the intranasal elevators used to advance the mass as the drill wires are placed at the base will keep the torn mucosal surfaces of the vault separated during healing and prevent adhesive obliteration of the anterior respiratory vault.

The lower half of the external nose is frequently injured without upper half fracture. The magnitude of this injury is often overlooked. Most of the distortion is intranasal. Externally, there may be no obvious displacement—only swelling and tenderness. A palpating finger must always be run down the nasal dorsum (Fig. 6). A soft point immediately caudal to the end of the nasal bones means that cartilaginous septal fracture and dislocation have occurred (Fig. 7). Intranasally, septal swelling will fill the nasal vestibules. This is due to a ballooning hematoma between the septal flaps (Fig. 8A and B). An early intranasal open reduction of this injury is mandatory (Fig. 8D). Lack of diagnosis and neglect result in external nasal deformity and septal airway obstruction (Fig. 8C). Rhinoplastic surgery for the deformity of neglected upper nasal injury is uniformly satisfactory. Rhinoplastic and septoplastic surgery for correction of lower half injury is always a compromise. Once the dorsal ridge hematomatous soft spot absorbs and organizes, the inspiratory vault of the nasal vestibule is forever lowered (Figs. 8C and 9). Though the later plastic correction obliterates the saddle of the dorsum and narrows the accordioned septum, it cannot restore the height of the intranasal fornix. Diagnostic X-ray is useless in this injury. The keys to diagnosis are the soft spot in the lower half of the nasal ridge into which the palpating finger falls as it slides down the nasal dorsum and the complete obliteration

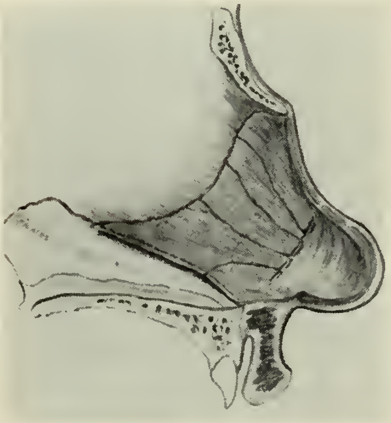


Fig. 9. The relative nasal "hump" resulting from lowering of the cartilaginous dorsum as a result of dislocation and comminution of the septal cartilage

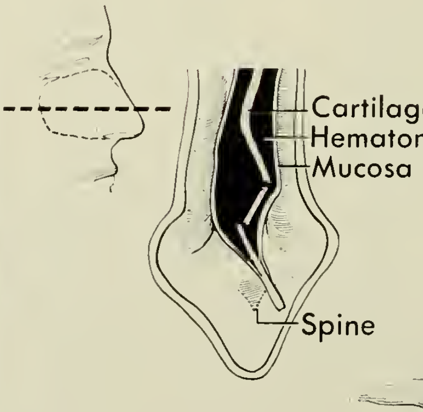


Fig. 10. Comminuted fracture dislocation of the cartilaginous septum resulting from blow delivered to the caudal end

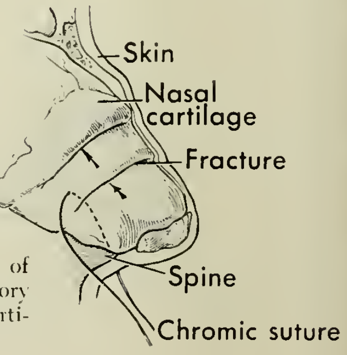


Fig. 11. Chromic suture transfixion of the cartilaginous septum prepatatory to anterior traction-reduction of cartilaginous fracture in Figure 9

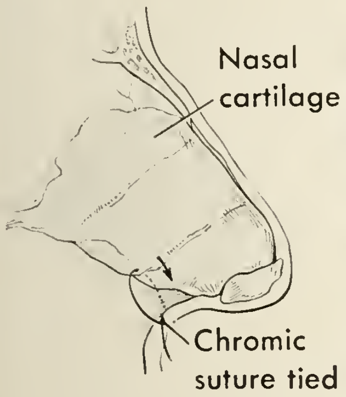


Fig. 12. Closure of suture passed through the nasal vestibular floor to embrace the anterior nasal spine and "unpleat" the accordion fracture of the quadrilateral cartilage

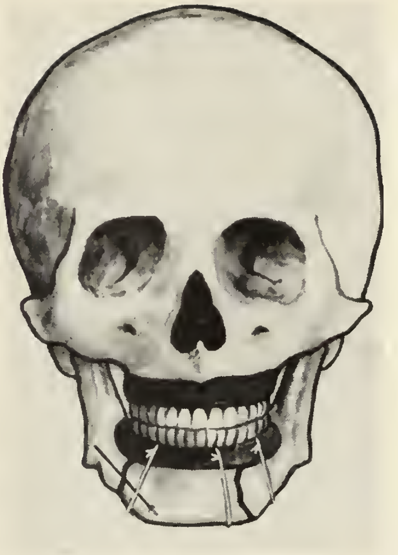


Fig. 13. Circumferential wire fixation to lower denture "splint." Fracture line posterior to the circumferential wire must be stabilized by internal pin as shown or by open loop wire placement at the free border.

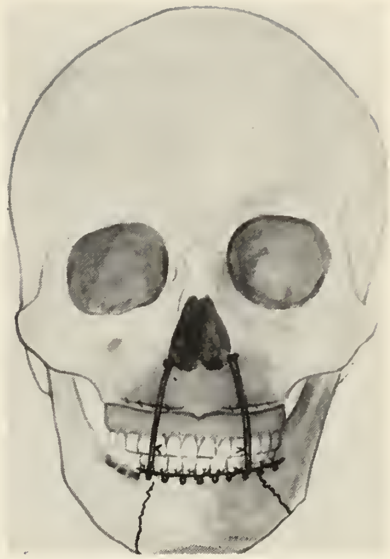


Fig. 14. Method of intermaxillary fixation to the edentulous maxillae by means of suspension wires looped through pyriform aperture drill holes and brought down through canine incisions

of the nasal airway by the hematoma between the septal flaps.

Septal incision as for a classic submucous resection evacuates the subperichondrial hematoma and exposes the multiple fragments of cartilage. Successive replacement of fragments from dorsum to floor is maintained by mattressing chromic sutures through mucosal flaps and cartilage at each fracture line (Fig. 8D). This restores the anatomic relationship of the quadrilateral fragment jigsaw and binds the mucoperichondrium to the cartilage to preclude postoperative hematoma and position change.

Where the injurious blow has been delivered not at the dorsum but at the caudal end of the nose, lip contusion, sometimes upper incisor tooth and alveolar fracture, and quadrilateral septal cartilaginous and anterior nasal maxillary spine fracture and displacement are not uncommon. The cartilaginous septum is accordioned posteriorward (Fig. 10). Palpation of the columellar end shows the absence of firm septal edge (Fig. 6). Reduction of the posteriorward accordioning will not maintain without loop suture fixation. This is accomplished by inserting a far posterior septal chromic transfixion suture (Fig. 11) which is brought forward and passed through the vestibular floor skin beneath the spine and into the opposite vestibule and drawn taut to "unpleat" the accordion (Fig. 12).

The mandible. The mandible may fracture in its vertical or its horizontal segments. Multiple fractures are common. Distortion of a side blow can fracture the impact point on the horizontal ramus and opposite vertical ramus at the thin condylar neck. Direct impact can fracture the symphysis and one or both condylar necks. Fracture through the tooth-bearing portion is usually compounded into the mouth along the line of a tooth or through the tight mucoperiosteum of the edentulous jaw. Disposition of fractured fragments is governed by direction of impact and pull of attachment of masseter and temporal, internal, and external pterygoid muscles.

Pain, swelling, malocclusion, and disturbance of articulation suggest the diagnosis of mandibular fracture. Visualization and palpation of intraoral compounding, hematoma, and crepitus lend confirmation as do X-ray studies.

The preferable method of reduction and fixation of a mandibular fracture is governed by the presence or absence of teeth and the location of fractures. The objectives are good dental occlusion and articulation and firm bony union.

Anterior fracture of the horizontal segment of the mandible in the presence of reasonably good teeth presents no fixation problem. Intermaxillary fixation by loop wiring or arch bar suffices.

Simple loop wiring techniques are readily mastered. When arch bars are used in preference to loop wires, a cardinal rule should rarely be violated—do not cross fracture lines with continu-

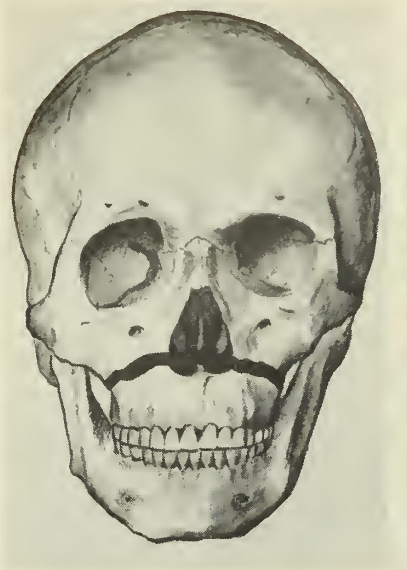


Fig. 15. The characteristic transverse maxillary fracture resulting in a freely floating palatal segment and facial elongation

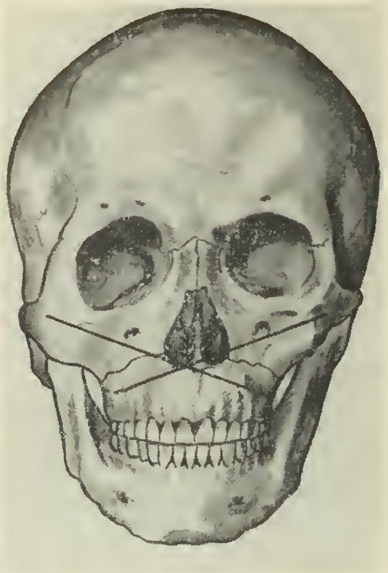


Fig. 16. Crossed-transfixation pins for stabilization and closure of gaping transverse palatal fractures. A similar horizontal transfixion is useful for an occasional flail malar fracture with comminutive loss of support bone.

ous arch bar but, rather, the arch bar should be divided at each fracture line.

The edentulous mandible or maxillae or posterior vertical fragment poses a special problem as does a subcondylar or condylar neck fracture. Open reduction and direct wiring through external approach are effective in some cases.

When the fracture line passes through a tooth space, the tooth can usually be preserved. Though the fracture line opens at the gingival margin to allow mouth bacterial contamination, oral hygiene, antibiotics, and immobilization usually facilitate normal healing and retention of the tooth. If retention of the tooth causes local reaction, the tooth can be removed at any time. Fracture through the tooth usually destroys its vitality, and removal as a part of the primary procedure is sometimes advisable.

The only tooth on a posterior mandibular fagment is particularly valuable as a means of controlling the vertical ramus. If it can be retained for four weeks to save the vertical dimension by occluding against the upper posterior teeth, it can accomplish as much as would an open reduction and wiring at the free border. The latter is usually necessary in the alignment and fixation of the posterior mandibular segment when the fracture line passes posterior to the last tooth. Direct loop wiring at the free border must be supported by supplementary intermaxillary fixation.

Whenever open, direct wiring at the free border is used, care must be exercised to preserve the inframandibular branch of the facial nerve. This open incisional approach is useful for direct wiring, but dissection should be kept to the minimum necessary for good access. Periosteal stripping is unwise. The physiology of bone healing should be enhanced by the procedure, not grossly handicapped by slovenly techniques, wide stripping, crude drilling, and further displacing during manipulation.

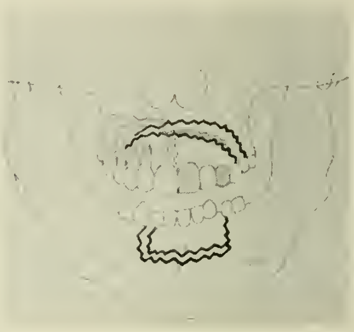


Fig. 17. Segmental alveolar fractures with peril to the nerve and vascular pedicle of contained teeth

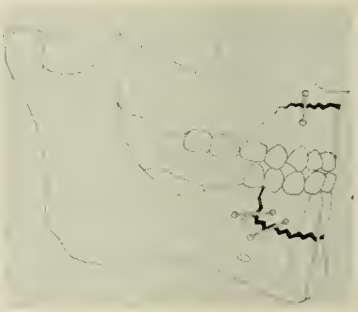


Fig. 18. Direct wire fixation of alveolar segments not satisfactorily controlled with simpler techniques

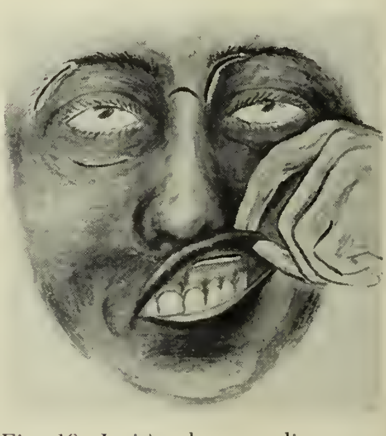


Fig. 19. Incisional access lines providing direct exposure for anatomic reduction and wire loop fixation

The edentulous mandible is often frail and, to a degree, atrophic. Drilling and pinning injury are usually undesirable. Circumferential wires unifying the mandible and the lower denture make for good splinting and early motion for mastication (Fig. 13). This is particularly favorable to nutrition of older edentulous patients.

When the posterior fragment cannot be looped in a circumferential fix, a supplemental free border loop or a pin can be incorporated. This additional injury should not be inflicted unless vertical ramus displacement is uncontrollable. Intermaxillary fixation for several weeks is desirable to stabilize this posterior fracture.

If the maxillary teeth are absent, intermaxillary fixation is best provided by direct wiring by loop through drill holes in the skeletal margins of the pyriform aperture. This same fix is useful for mandibular fractures when mandibular teeth are present and maxillary are absent. In this instance, the pyriform loops attach to mandibular arch bars rather than to the circumferentially fixed mandibular denture (Fig. 14).

Fractures of the condylar neck with or without dislocation of the head should be treated simply. They should be placed in rest position with intermaxillary or bandage support for the acute painful period. Early motion is vital to the best functional result. The temporomandibular is not a "close-approximating" joint. It is rather a guide to the mandibular, antigravity chewing motion. This loose "guide" function is provided after unilateral neck fracture healing even though union at the neck is incomplete or the head is displaced. The main deterrent to a good functional result is unwise and prolonged immobilization. In this regard, the "treated" patient can have a worse result than one who has had no treatment at all. A few days to a week of immobilization is adequate except when other mandibular or maxillary fractures demand compromise.

The treatment of combined neck and ramus fractures should be that which will allow the earliest and fullest motion compatible with assured union of the latter. This may demand an open wiring of the horizontal ramus, instead of "simple" intermaxillary fixation. Better still, in many situations, is binder intermaxillary fixation which the patient can remove and replace daily after the first several weeks of callus formation, favoring motion at the condylar fracture and support in good alignment for the associated ramus fracture for alternate parts of each day.

Bilateral fracture of the condylar necks is a major problem. Retrusion of the mandible and loss of vertical dimension result. If at least one condyle is not grossly displaced, the situation can be saved by intermaxillary fixation to the point of early union on this side. Intermaxillary binder maintenance is then used at night and free motion by day for at least several months. The mandibular arch bars are not then removed, while a two-week "trial of maintenance" period demonstrates that no retrusive tendency exists without the nocturnal binder traction.

When both condyles are grossly displaced, the vertical dimension should be restored on at least one side by open reduction. If alignment and fixation on the one side are very good, such treatment of the second side—the worse of the two—need not be attempted. These are difficult, technical-surgical problems and the second side may not enhance the end result if its dislocation is more extreme and its reposition not fully satisfactory. The restoration of the vertical dimension on one side will avoid retrusion and will act as an adequate guide to occlusive chewing. Anatomic reduction may require submandibular access for digital manipulation. The direct application of wire loop fixation to the fracture neck is usually effected through preauricular or endaural exposure. Early motion is the key to good function. Intermittent binder application after the first few weeks will facilitate this.

There are limitless appliances and techniques for mandibular fractures of unusual type. Amidst all this maze of gear and method, the novice can flounder in confusion. He frequently adds a few of his own screws and bolts until experience reorients him to virtues of the simple and direct.

The maxillae. The tooth-bearing palatal segments of the maxillae suspended as they are by thin bony laminae from the complex of the middle facial third are frequently broken free. The impacting forces resulting in a floating palate can, by posterior displacement, fracture the vertical plates of the pterygoid and palatal bones. By locking posteriorly, these bones may prevent forward reposition of the entire palatal complex.

Unlocking requires downward traction of the posterior bony palate and is not possible by interdental traction. A solid, sharp bone hook with a 1.5- to 2-cm. curvature passed upward through the soft tissue junction of soft and hard palates so the point comes to lodge on the postchoanal floor will allow the downward directional pull to disimpact. Rocking traction with a lion jaw forceps applied at the same time to the anterior alveolus or with a special intranasal-intraoral grasping forceps will combine to mobilize freely and to advance the whole palate. Intermaxillary fixation with binders or wires between arch bars will then fix and occlude.

The palate may displace as a unit or it may fragment. In any case, realignment of all fragments with the opposite mandibular segments and fixation with the intermaxillary wiring result in good functional and cosmetic healing.

Where the weight and pull of the combined mandibular and palatal mass open the transverse fracture line and elongate the face (Fig. 15), fixation to the upper skeleton can be effected with either direct wire loops at the pyriform aperature buried through buccal canine incisions or crossed transfixion pins (Fig. 16). These latter must be sufficiently stout as not to "willow," else the pin can strike a firm bony segment and take an unwanted curve into the orbit. Skewering the globe could detract from the final result.

Alveolar ridge fractures. Tooth-bearing segments of the alveolar ridge may be completely fractured and hinged on the mucosa or may be fractured incompletely in various degrees and with variable injury to contained teeth (Fig. 17). Conservation is the keynote in management. Without loss of time, the segment should be fixed in anatomic position and buccoalveolar sulcus restored by careful mucosal approximation.

Simple methods of fixation with arch bar, tandem wiring, or circumferential wiring usually give good protection and fixation. Intermaxillary occlusive techniques insure position. An occasional special circumstance demands direct wiring (Fig. 18) or silver cap or acrylic splints. Most teeth will be conserved by these methods. The experienced surgeon has dread aversion to the sacrifice of teeth and tooth-bearing segments.

"Central-third" fractures. The pyramid in the center of the middle facial third is comprised of the maxillae; the nasal, lacrimal, and ethmoidal bones; and the intranasal vomerine and inferior conchal bones. Straight, forceful projection of the face into an unyielding receiver may impact the nasomaxillary mass with or without free fracture of the palatal segment.

Advancement techniques by postpalatal hook, intranasal-intraoral grasping forceps, and intranasal elevator can be supplemented by "molding" pressures deep to the inner canthal areas to reform the crushed ethmoid mass. Free segments of the frontal processes of the maxillae can best be retrieved from the nasal space and repositioned by "bimanual" manipulation with the fifth finger deep in the nasal vault and the fingers of the opposite hand along the orbital rim. Precise replacement can be further assured by infraorbital incision in the lower crease of the orbicularis oculi and direct visualization (Fig. 19). This allows wire loop fixation at this point, either single or multiple as necessary to complete the reformation of the infraorbital rim and its union to the nearest solid lateral abutment (Fig. 20).

In the glabellar area, similar incisional view of the nasal root (Fig. 19) and direct wire loop can be valuable in fixing the pyramid to the frontal skull base if gaping requires closure (Fig. 20). This can be combined with nasal mass transfixion and molding with lateral malleable metal splints when bony nasal mass is "eggshelled" (Fig. 5).

It is important to disimpact the recessed nasomaxillary mass at the first opportunity. Early fusion occurs. A bulging of the ethmoidal labyrinth and retrocession of this central mass are impossible to correct by later plastic repair. Bony union occurs in weeks due to thin plates, extensive periosteal surfaces, and rich blood supply.

When this type of fracture includes fracture of the cribriform plate and cerebrospinal fluid leak, early reposition is particularly imperative. The breach in the floor of the anterior cranial fossa will more readily and surely heal and seal if anatomic reposition has been accomplished. If stereoscopic skull films demonstrate a bone fragment displacement and intrusion into the anterior fossa, the facial realignment should be performed in conjunction with intracranial removal of the intruding bone from the floor of the anterior cranial fossa. This latter procedure is accomplished neurosurgically by hairline incision and lowering of the total forehead flap.

Whatever the upper aspect of the pyramidal fracture demands for repositioning and fixation, at the intermaxillary level, the teeth must be fixed in occlusion. Arch-bar application provides a good means. If there is no concurrent mandibular fracture, the versatility of the arch bars allows intermittent use of the intermaxillary elastic binders during the late healing period.

Fractured edentulous maxillae present no occlusion problem whether the mandible has teeth or not. Intermaxillary fixation is not necessary. Anatomic reduction and direct fixation can be followed by denture revision after healing.

The malar bones. Laterally, the malar bones form the buttress and contour of the cheeks. The human has a marvelously rapid protective reflex that turns the head at the instant of impact. The brunt of many blows is borne by the malar bones. Their attachment points—frontal, temporal, and maxillary (infraorbital and alveolar)—are weaker than the body of the bones (Fig. 21). Only occasionally is the bone fragmented. Displacement, however, can be extreme because the large underlying maxillary sinus space provides no support. Rapid swelling tends to obscure the true extent of the cave-in. The line of fracture in the orbital floor tears the periorbita. Hematoma sup-

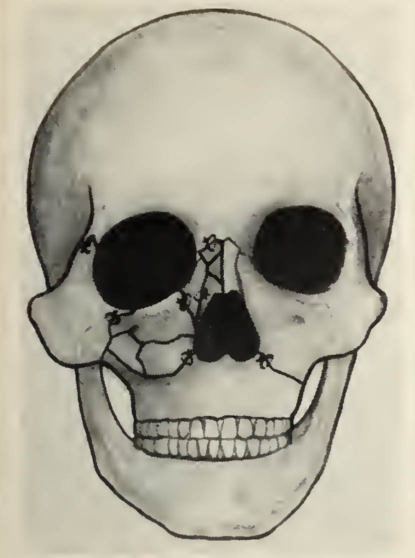


Fig. 20. The maintenance of anatomic realignment with permanent wire loop fixation

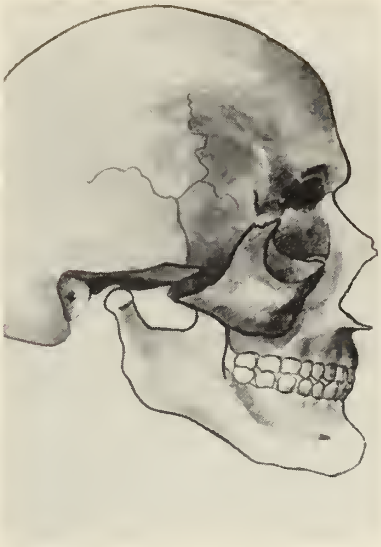


Fig. 21. The fracture zones of the abutting malar-maxillary complex

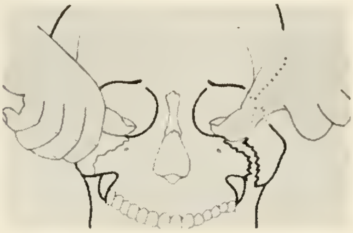


Fig. 22. Method of examining the infraorbital rim for malar fracture with comparative thumb palpation from position behind the patient

ports the globe at normal level for a week or two, but when it resorbs, the globe drops. This global displacement and the shift of the bony attachment of the inferior oblique muscle can result in diplopia of very disabling character. The same hematoma dissects under the bulbar conjunctiva to the limbus. This subconjunctival hemorrhage should warn the examiner that here at least is one swollen and ecchymotic eye that should not be made the butt of doorknob jokes. The humor loses much of its flavor when a patient returns in two weeks with a flattened face and diplopia.

A chin-nose position film as of the maxillary sinuses is quite diagnostic of malar fracture. The presence or absence of displacement should not be determined finally by the film, however. Its angle may not define significant malposition. The palpating thumb placed along the infraorbital edge may reveal a step-down that is not well shown on the film (Fig. 22).

Since the weak point of fracture on the infraorbital rim is at the infraorbital foramen, hypesthesia of this sensory nerve is usual with malar fracture. Hence, numbness of the upper lip and nasal ala on the side of the injury is an important diagnostic sign. So also is the presence of blood

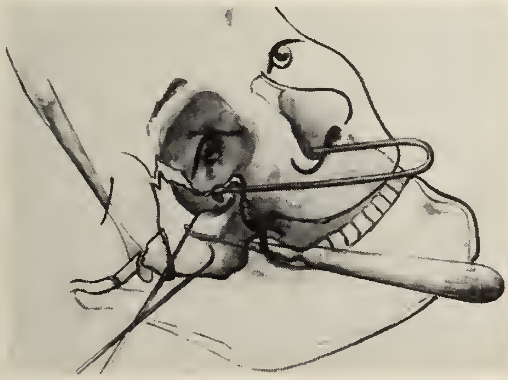


Fig. 23. Techniques of malar fracture realignment. Reversal of the injury force is the basic objective.

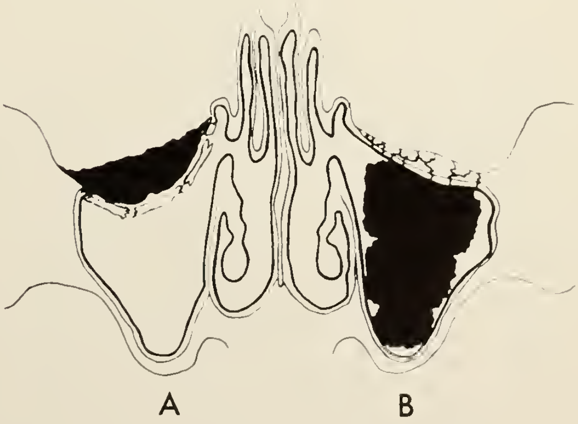


Fig. 24. [A] Orbital floor implant with silicone rubber sponge insert for long-standing orbital floor depression. [B] Intramaxillary antral support of recent orbital floor ("blowout") fracture with indwelling silicone rubber palisade in three insertional layers

in the maxillary sinus due to tear of the mucoperiosteum. Sufficient depression of the malar arch can impinge on the mandibular coronoid and mouth closure will then be difficult.

Reposition of the malar bone can be accomplished in several ways. There is no best way for all fractures. The objective of reversing the injury force to realign the fragments demands familiarity with a number of approaches (Fig. 23). A lateral blow can be reversed through a temporal hairline and temporal fascia incision with the elevator placed beneath the malar arch. Inferior displacement of the body can sometimes be corrected by manipulation with a bone hook externally or elevation in the buccal sulcus intraorally. Posterior impaction of a substantial fragment of the infraorbital rim may require direct exposure through a well-placed infraorbital incision and retrieving of the fragment with a short strong hook. This exposure allows direct wiring across the fracture line. As with nasomaxillary fragmentation, this is accomplished with a drill, fine drill points, and fine steel wire loops (Fig. 20).

It is inadvisable to attempt manipulation of the malar bone with a towel clip. This endangers facial nerve filaments when the tenaculum slips. Entering the maxillary sinus through the canine fossa is necessary only in special instances. The maxillary opening requires sacrifice of bone in opening the sinus that would be advantageous for support of the repositioned malar.

If the comminuted shell of the orbital floor is lost into the maxillary antrum ("blowout fracture"), it is better to use incisional access to elevate the orbital contents and visualize the fragmentation directly. Canine fossa opening for digital manipulation and elevation of the fractured segments may be helpful. The inferior oblique muscle and attachment must be anatomically replaced. Three-segment, palisade, intra-antral support with fine, closed-mesh silicone rubber sponge left in place six to ten weeks will eventuate in a good result (Fig. 24B). If support fragments are deficient, the orbital floor can be supplemented with a properly placed silicone rubber sheet (Fig. 25). If necessary, infraorbital rim fragments are wired directly into place (Fig. 20).

Occasionally, the frontomalar fracture line will not hold in anatomic reposition after reduction. Direct wiring to the frontal abutment through a lateral brow incision (Fig. 19) with or without infraorbital wiring (Fig. 20) is then useful. On rare occasions, it can be supplemented with binder traction from a screw inserted in the body of the bone to a headcap appliance. An impaling Kirschner wire carried across to firm supportive bone on the opposite side is sometimes a simple and useful fixation method.

Solid healing in malposition due to neglect of the acute malar fracture is best corrected by osteotomy refracture along the four main fracture lines and reclamation of the malar bone itself

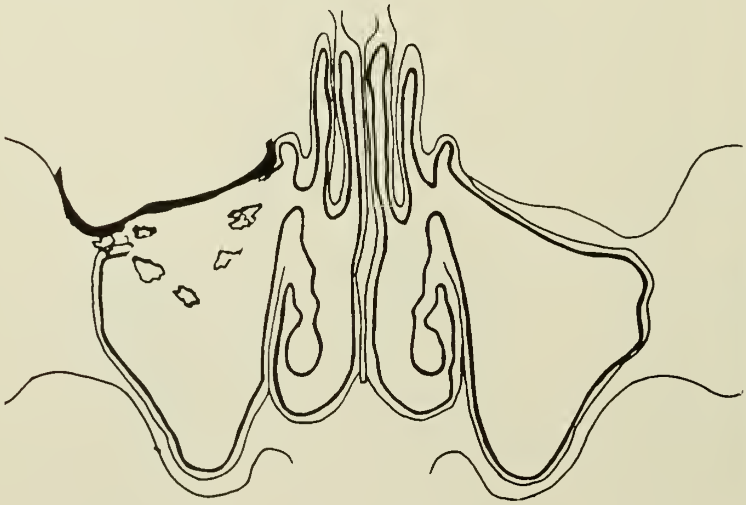


Fig. 25. Silicone rubber sheet substitution for loss of orbital floor fracture fragments in acute injury

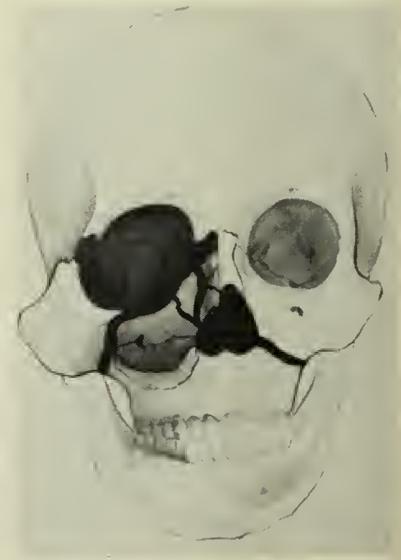


Fig. 26. Complex facial injuries may be unilateral, as above, or bilateral. The mandible may or may not be involved. The whole problem is divisible into individual component parts—each amenable to relatively simple solution.

for replacement and direct fixation (Fig. 20). Results are usually superior to those obtained by implantation of iliac bone or diced cartilage.

When the position of the main body of the malar-maxillary complex poses no problem but long-standing orbital floor deficiency cripples ocular fusion and disables cosmetically, elevation and support can be helpful. This may be effected with autogenous or despeciated bone implant or silastic sponge implant. The latter is shaped and then divided into two segments by anteroposterior division. One half is inserted through a medial two-third infraorbital working incision and crowded with its taper laterally. Then, the medial half is inserted and the cut edges matched along the division line (Fig. 24A).

Complex fractures. The challenging injuries of the facial skeleton are those that combine injury to all or most of the component bones (Fig. 26).

Multiple fractures of the facial skeletal components or total fracture are not uncommon. Extraordinary disruption is compatible with life and occasionally occurs in the absence of intracranial or other injury.

Direct inspection, palpation, and X-ray study serve to orient one with the problem and define the repair sequence. The order of treatment is airway establishment, blood replacement, general assessment, adequate restorative pause, and, then, integration of the reparative procedures in one orderly operative sequence.

Skeletal repair techniques should not be inordinately complex. Simplicity in reduction method and in fixation methods should be the rule. A certain amount of gadgetry is necessary. It can be grossly overdone, and then the apparatus becomes more a problem than the injury. A "Rube Goldberg" solution is a poor substitute for simple direct fracture exposure and wire loop or pin fixation. Incisional access (Fig. 19) will expose the usual fracture sites directly. Anatomic realignment with direct vision is more certain than is tactile realignment through an edematous, ecchymotic, soft tissue mass. Permanent wire fixation is accomplished through the incisional exposure with fine loops passed through fine drill holes (Fig. 20). In multiple fractures, the most lateral or superior fragment is attached first to the unfractured skeleton. The others are attached in succession—downward and medialward.

Larynx and hyoid bone. When the larynx or hyoid bone is fractured, the patient's survival usually hinges on a reasonably prompt tracheotomy. Some patients do survive without tracheotomy or recognition of the true nature of their injury only because of a less severe injury.

The respiratory embarrassment and hoarseness as well as the contusion and tenderness in the anterior neck are ample evidence of traumatic intralaryngeal mischief. Pain with swallowing and phonating is common. Bloody expectoration indicates mucosally compounded fracture. These evidences are indications for intralaryngeal investigation even though immediate tracheotomy is not essential. Early correction of laryngeal damage is vital to the preservation of a good voice. The arytenoid cartilage may be dislocated from the cricoid. Since the vocal cord is attached to the arytenoid, reduction of the dislocation can restore some motion if organization in malposition is not permitted. On the other hand, fracture of the thyroid cartilage tears the attached vocal soft parts and may even compound through them into the airway. Moulding the cartilages into anatomic position can be aided by insertion of an endoscopic tube through the larynx. More often than not, this maneuver must be amplified by exposing the external aspect of the larynx and verifying the realigning of fragments directly. A collar incision with reflection of overlying soft tissues provides this direct view. An indwelling silicone rubber sponge mold placed in the laryngeal lumen to encourage the resorption of hematoma and adherence of perichondrial flaps can be important in preventing intraluminal stenosis.

Delay even for days, in all of the above, is disastrous. Once the soft tissues of the vocal apparatus have foreshortened and organized, they are forever lost for normal vocal function. Late coring and grafting provide a poor substitute for the restoration of early reduction.

SUMMARY

An open airway is the paramount primary problem in severe facial injury. Assessment of associated injuries and general restorative measures have priority over facial repair. Soft tissue repair requires overall precision exemplified by use of magnification. Lack of excellent skeletal alignment and fixation dooms the best soft tissue restoration to failure. Laryngeal injury results in airway embarrassment or hoarseness and local pain and tenderness, or both. Prompt evaluation and treatment can save life or crippling malfunction.

Management of Thoracic Injuries

JOHN F. PERRY, JR., M.D., Ph.D.
St. Paul

THORACIC TRAUMA is an important part of the multiple injury syndrome. Blunt chest injuries occur in association with other injuries more frequently than do penetrating thoracic wounds. In our experience, 101 or 60.8% of 166 patients with blunt chest trauma had damage to other parts of the body;[1] only 8 or 20.5% of 39 patients with penetrating chest wounds had such injuries.[2] The diagnosis and management of chest injuries in general and the problems presented by trauma to the chest of the patient with multiple injuries are considered in this paper.

Thoracic injuries can be classified into several categories on the basis of anatomical derangement. These include penetrating wounds, single or multiple rib fractures, hemopneumothorax, flail chest, lung contusion, rupture of the diaphragm, laceration of the great vessels or heart, rupture of trachea or bronchus, esophageal injury, and cyclothorax from injury of thoracic duct. Blunt trauma may produce any and all of these manifestations; however, injuries of trachea and bronchi are uncommon and those of esophagus and thoracic duct are extremely rare in patients who survive long enough to reach a hospital alive. Penetrating chest wounds are usually due to bullet or knife and ordinarily do not produce sufficient injury to the bony thorax to result in a flail chest. Diaphragmatic hernia secondary to penetrating wounds of the chest is likewise uncommon. The other types of thoracic trauma listed above may be produced as a result of penetrating chest wounds.

Although division of chest injuries into the above descriptive categories serves as a basis for discussion of treatment, such a classification does not indicate the physiologic derangements which are produced by the injury. Loss of circulating blood volume from hemorrhage and loss of ventilatory capacity of the lungs are the principal defects resulting from most chest injuries. Less commonly, intrathoracic sepsis may result from esophageal rupture or from abdominal visceral injury occurring in association with diaphragmatic rupture. The great majority of thoracic injuries which produce a fatal outcome do so because of shock due to hemorrhage or from interference with ventilation. The immediate goal of emergency treatment of the thoracic injury is correction of these two defects.

DIAGNOSIS OF THORACIC INJURY

A history of the mechanism of injury is important. Penetrating chest wounds usually result from stabbing or gunshot; less commonly they are due to other causes such as falling objects or traffic accidents. Blunt thoracic trauma occurs most commonly to auto occupants involved in accidents, to pedestrians struck by motor vehicles, and to persons injured in falling. Motorcycle or bicycle accidents, altercations, and industrial accidents result in a few blunt chest injuries.

The clothing must be completely removed from the patient's chest to allow for adequate physical examination. Inspection of the chest will show contusions or abrasions, limited excursion of one side of the chest, obvious deformity, or paradoxical motion of a segment of chest wall. Difficulty in breathing, cyanosis of lips and nailbeds, use of accessory muscles of respiration, and flaring of ala nasi may be apparent. Palpation will demonstrate instability of a segment of chest wall, crepitus due to broken ribs, or subcutaneous emphysema. Percussion is useful to elicit the tympany of tension pneumothorax or the dullness due to a blood-filled hemithorax. Auscultation is primarily useful to determine presence and character of breath sounds and to indicate rales which may be due to pulmonary edema, blood, or gastric content in the tracheobronchial tree. Since the physical examination of the chest of a seriously injured patient is usually conducted with the subject supine, an injury may be present and no abnormal physical signs may be elicited from such a limited examination. For example, a large volume of blood may be present in the chest and not be detected by

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JOHN F. PERRY, JR., *is chief, Department of Surgery, St. Paul–Ramsey Hospital, St. Paul, and professor of surgery, University of Minnesota Medical School.*

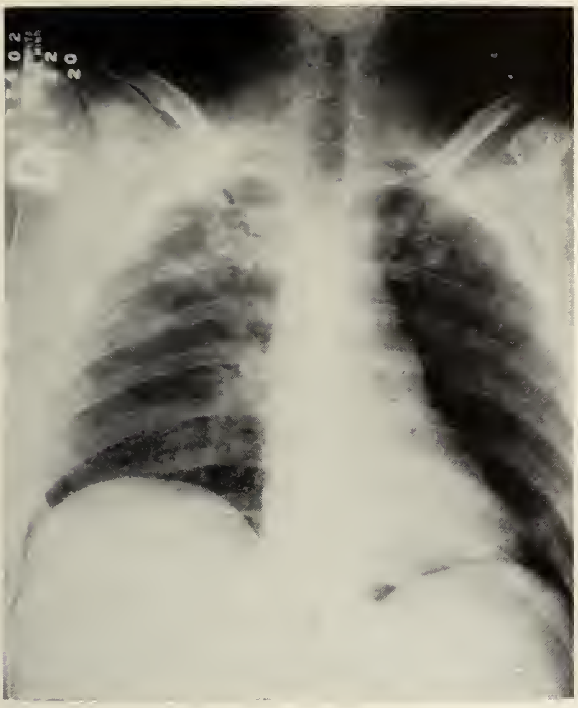

Fig. 1. Only a slight difference in density of the two sides can be detected in this supine radiograph of the thorax, despite a large quantity of blood present in the right chest cavity.

physical examination carried out under these circumstances.

Laboratory examinations provide little help in early diagnosis of chest injury. Hemoglobin values are usually normal even in the presence of obvious hemorrhagic shock. The white blood count may be normal; it may be elevated due to the chest injury or to other causes. Under most circumstances, leukocyte counts provide little aid in deciding if a thoracic injury is present.

Radiographic examination of the thorax is an essential part of the diagnostic work-up. Upon arrival at our hospital, the seriously injured patient is usually placed on a padded plywood board for examination and for resuscitation. Supine chest X-rays can be made, but upright films are not obtainable initially if the patient is in shock or unconscious, or if the patient has spine or multiple injuries. When the patient's condition permits, upright chest films should be obtained since they provide additional valuable information. Specific radiographic findings are discussed with the various injuries in the following sections.

The injured patient admitted to the emergency room with a low or absent blood pressure is almost always in this condition because of loss of his circulating blood volume. The site of bleeding must be determined as rapidly as possible after hospital arrival. Blood loss from external wounds, bleeding into soft tissues around fractures of long bones or pelvis, or hemorrhage into abdomen or chest is responsible for the arterial hypotension. If blood loss cannot be accounted for by external hemorrhage or bleeding into fracture sites or into the peritoneal cavity, then the chest is the likely site of hemorrhage. Chest X-ray usually demonstrates the hemothorax. However, supine radiographs of the chest may show only a slight difference in density of the two sides even when a large volume of blood is present in one hemithorax (Fig. 1). Diagnostic thoracentesis performed in the posterior axillary line with the point of the needle angled toward the gutter will demonstrate any significant collection of blood in the chest of a patient lying supine. If profound shock is present on admission and is unresponsive to rapid blood volume replacement, thoracentesis is the most rapid means for determining if hemorrhage into a pleural cavity is responsible.

GENERAL PRINCIPLES OF TREATMENT OF CHEST INJURIES

The majority of chest injuries are treated without recourse to open thoracotomy. Exceptions to this rule will be discussed. As stated before, restoration of blood volume and the ventilatory capacity of the lungs are the first goals of treatment. [1] Patients admitted in shock from intrathoracic bleeding require rapid blood volume replacement. We utilize low-titer, O-negative blood without cross match for resuscitation of the injured patient admitted in shock. Blood typing is carried out at the same time. As soon as type-specific, cross-matched blood is available, it is utilized. Hemorrhagic shock is a frequent cause of early death of the patient with multiple injuries and the patient with chest trauma. Replacement of blood volume cannot be delayed. Vasopressor drugs and volume expanders such as dextran are not adequate substitutes for blood. [2] Chest tubes (intercostal suction catheters) are utilized to remove air and blood from the chest. Ventilatory capacity is restored since the lung is immediately reexpanded and the rate of bleeding can be monitored. Large-bore chest tubes are utilized so that occlusion by clot does not occur. For adults, size 40 to 44 F plastic catheters are adequate. Smaller catheters can be utilized for children. [3] The endotracheal tube serves as a means for rapidly establishing an airway and as a route for artificial ventilation until definitive arrangements for an airway are made. Tracheal suction and tracheobronchial lavage

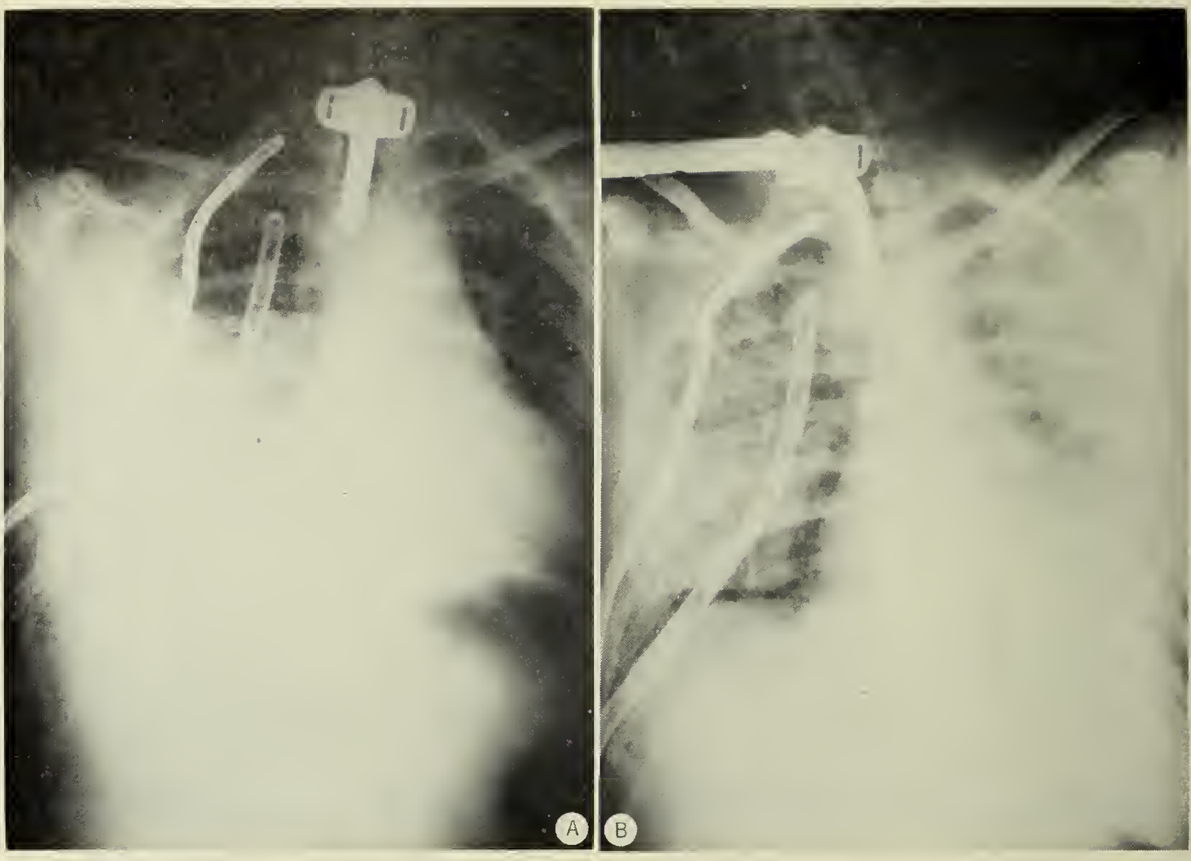

Fig. 2. [A] Flail chest injury. Chest X-ray taken soon after admission and initial treatment. Opacity on right side is due to hemothorax and contused lung. [B] Chest X-ray taken twelve hours later shows massive bilateral pulmonary edema. Paradoxical motion of the flail segment had not been adequately controlled in the interim. Metallic foreign bodies over sternum are Bigelow screws which were placed in an attempt to stabilize the flail segment by traction. These are no longer utilized.

can be carried out by this route. [4] Tracheostomy is utilized in chest injuries to provide a means for long-term support of ventilation by mechanical respirators, as a route for tracheal suction and tracheobronchial lavage, to decrease airway resistance, and to reduce dead space ventilation. [5] Thoracentesis is employed in some circumstances for the diagnosis of hemopneumothorax rapidly and in selected patients for its treatment. [6] Intercostal nerve blocks using procaine hydrochloride (Novocaine®) or lidocaine (Xylocaine®) serve to reduce pain from broken ribs and increase their excursion during respiration. Unfortunately, relief is usually short-lived and the procedure must be repeated often to be effective. [7] Ventilation and fixation of the unstable thorax is achieved through control of respiration using mechanical respirators. Intermittent positive pressure machines such as the Bennett, Mörch, Bird, and Engstrom respirators have all been utilized successfully. External traction with towel clips or screws or splints and struts to fix unstable segments of the chest wall was used in the past but is no longer employed. [8] Tracheobronchial lavage[3] with warm saline is used to remove blood, aspirated vomitus, and secretions from the tracheobronchial tree. The above includes only those techniques and procedures which specifically apply to the treatment of chest injury. Obviously, other supportive measures for relief of pain and to prevent infection are utilized as in management of traumatic injuries in general.

TREATMENT OF SPECIFIC THORACIC INJURIES

Fractured ribs. Fracture of a single rib usually poses no problem other than pain. Strapping the chest with adhesive tape or binders to restrict motion is not employed since the effect produced, limited ventilation of the ipsilateral lung, is the exact opposite to that which is desirable. Intercostal nerve block is rarely indicated and pain relief is obtained with oral analgesics. The patient with multiple other injuries and a single uncomplicated rib fracture usually requires little specific treatment for the rib injury. Multiple rib

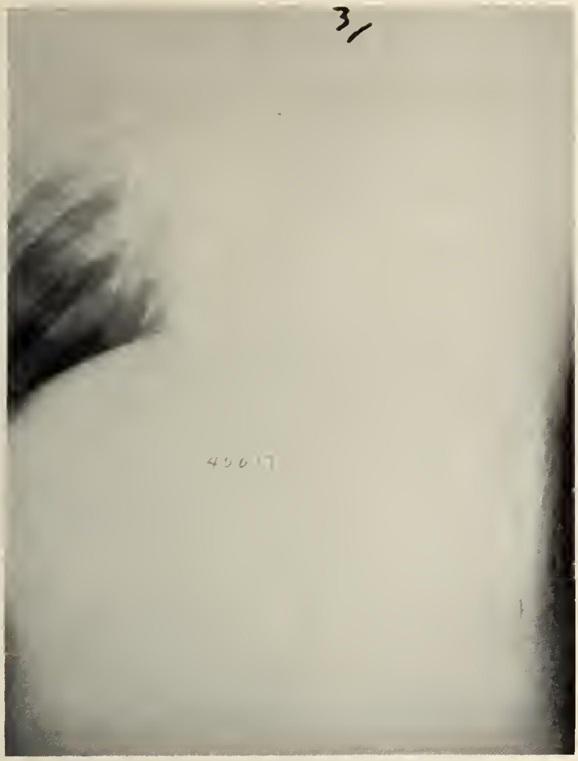

Fig. 3. Massive clotted hemothorax due to blunt trauma

fractures without complications such as hemopneumothorax or flail chest are deleterious primarily because ventilation of the lung on the affected side is decreased and coughing is voluntarily suppressed because of pain. Inadequate aeration and retained tracheobronchial secretions lead to atelectasis and pulmonary edema and the full-blown syndrome of the traumatic wet lung may be produced. Nerve blocks and analgesics to relieve pain may be helpful. Frequent tracheal suction by catheter is mandatory to clear secretions and stimulate coughing. Intermittent positive pressure ventilatory assistance by means of a tight fitting face mask and positive pressure respirator several times a day may be helpful. Tracheotomy, assisted ventilation by a respirator, and frequent tracheobronchial suctioning will usually be necessary if atelectasis and pulmonary edema are allowed to develop. Repeated physical examination of the chest and frequent radiographs are the best means for monitoring progress in the early period after injury. Dyspnea and cyanosis or the laboratory demonstration of a decrease in oxygen saturation of arterial blood in the absence of obvious cyanosis are indicators of perfused but inadequately ventilated areas of

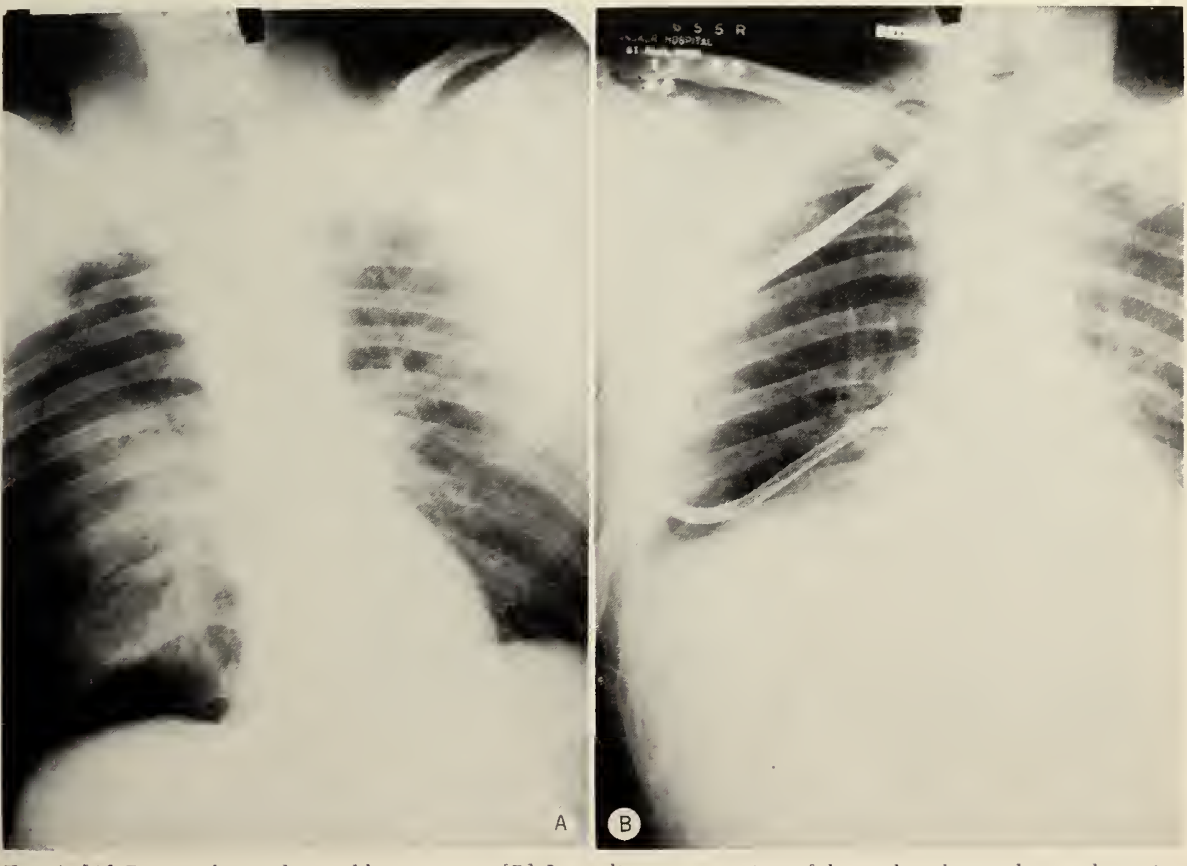

Fig. 4. [A] Pneumothorax due to blunt trauma. [B] Immediate reexpansion of lungs by chest tubes and suction

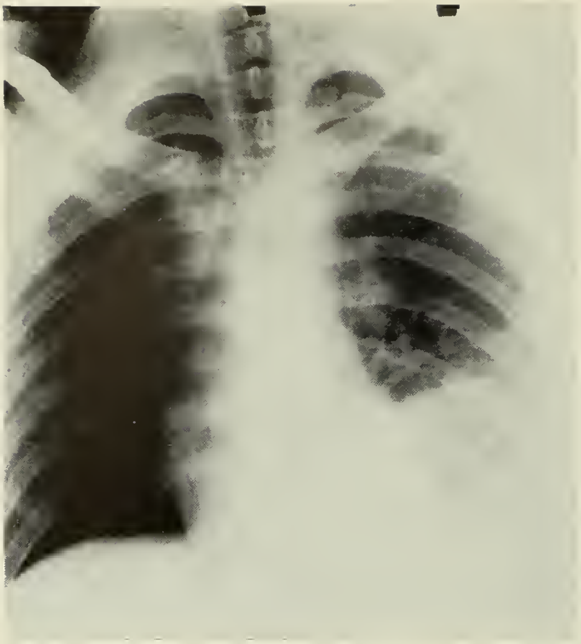

Fig. 5. Traumatic rupture of diaphragm. Air containing abdominal viscera is displaced into left chest. This might erroneously be interpreted as a high diaphragm.

the lungs and call for more vigorous treatment.

Penetrating chest wounds. Sucking wounds of the thorax require debridement and closure. If massive contamination of the chest wall and pleural space has occurred, limited thoracotomy may be necessary to remove organic foreign matter and for proper debridement. Most penetrating wounds of the thorax produced by knives and bullets in civilian life require debridement of the wounds of entrance and exit only and a chest tube to treat hemopneumothorax if present. Open thoracotomy is employed only if hemorrhage is massive or if the heart or other vital structures are injured as discussed in subsequent paragraphs. Metallic foreign bodies in the mediastinum and metallic foreign bodies greater than 2 cm. in diameter elsewhere in the thorax should be removed. This rarely requires an emergency operation, however.

Flail chest. An unstable segment of the chest wall develops because multiple ribs are fractured in two sites, multiple rib fractures have occurred in combination with costochondral separations, or bilateral costochondral separations and a sternal fracture are present. The unstable segment moves in paradoxical fashion with respiration and interferes with adequate exchange of air. Flail segments which are posterior or posterolateral in location usually produce less interference with ventilation than those flail segments in an anterolateral or anterior location. The most serious derangements are produced by sternal fractures and associated bilateral costochondral separations. Here the entire anterior aspect of the thorax may move in paradoxical fashion with breathing. Flailing or paradoxical motion of the unstable segment may be apparent at the time of hospital arrival. It may not develop until hours later when retained secretions have increased resistance to movement of air in the tracheobronchial tree and the decrease in ventilation caused by pain has led to hypoxia and increased respiratory efforts.

The majority of patients with flail chest injuries require tracheotomy and assisted ventilation with a mechanical respirator. An occasional patient whose flail segment is small may be treated adequately by tracheotomy alone. Rarely, a patient with a small lateral or posterior flail segment is first seen at a time remote from the injury, and it is apparent that significant interference with ventilation has not occurred. Tracheotomy and assisted respiration are obviously not required under this circumstance. It must be emphasized that untreated flail chest injuries with a benign clinical course are the exceptions and not the rule. Most flail chest injuries require vigorous treatment including assisted or controlled ventilation if hypoxia and lethal pulmonary edema are to be avoided (Fig. 2 A and B).

Hemopneumothorax is a frequent accompaniment of flail chest and is treated routinely by chest tubes and suction. Because of the likelihood of tension pneumothorax developing when positive pressure ventilation is utilized, all patients with flail chest who are to be treated by

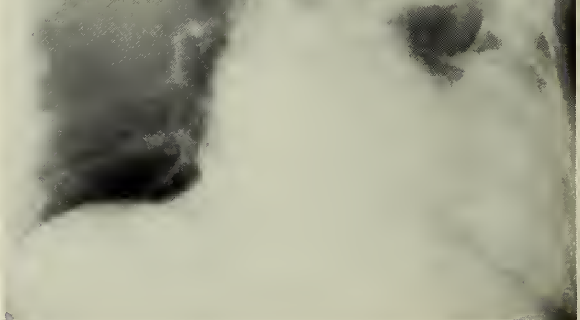

Fig. 6. Traumatic rupture of diaphragm. The radiographic appearance here is much more obvious than Figure 5.

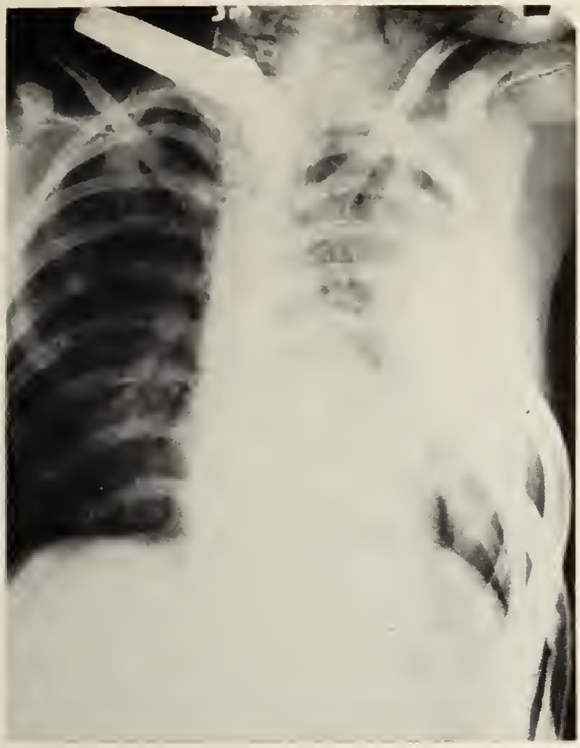

Fig. 7. Contusion of left lung due to blunt trauma. Chest tubes were necessary because of an associated pneumothorax. Bleeding into the tracheobronchial tree required tracheotomy, repeated tracheal suction, and tracheobronchial lavage over a period of several hours for survival.

mechanical respirators have intercostal suction catheters placed on the side of the chest with the rib fractures whether hemopneumothorax is present or not.

Control of the flail motion must be achieved by treatment. If spontaneous respiration with paradoxical motion of the flail segment continues, ventilation will continue to be inadequate and hypoxia will persist. It may be necessary to control the patient's breathing manually, using an anesthesia machine delivering oxygen until hypoxia is relieved. Inadequate treatment of the flail chest injury leads rapidly to pulmonary edema which is often irreversible. Patients with head and abdominal injuries are especially likely to develop this complication.

Hemopneumothorax. In our institution most patients with hemothorax who are seen early after acute chest injury have chest tubes placed to remove blood and reexpand the lungs. If continued bleeding occurs, this will readily be apparent. Only those patients who have isolated chest injuries with minimal to moderate hemothorax who are seen late after injury are treated by thoracentesis alone. Hemothorax is treated by early thoracotomy under the following circumstances: [1] initial recovery of 1,000 ml. or more of blood from the chest of a patient with unstable blood pressure, [2] clotted hemothorax with shifted mediastinum (Fig. 3), [3] continued bleeding of 200 ml. or more per hour from chest tubes, [4] massive hemothorax and shock unresponsive to blood replacement, and [5] most penetrating wounds of the heart.

Traumatic pneumothorax with few exceptions is likewise treated by placement of intercostal suction catheters (Fig. 4A and B). This is especially important in the patient with multiple injuries or the unconscious patient. Minimal (10 to 15%) pneumothorax unassociated with other injuries and not progressive as demonstrated by repeated chest X-rays usually does not require chest tubes. Pneumothorax due to bronchial rupture requires early thoracotomy.

Rupture of the diaphragm. Traumatic rupture of the diaphragm is usually the result of severe blunt trauma and characteristically occurs in association with other injuries. The radiographic manifestations of the injury may be clear-cut (Figs. 5 and 6), but diagnosis may be delayed if blood in the hemithorax obscures visualization of the dislocated abdominal viscera. Treatment is surgical repair of the torn diaphragm after replacement of viscera in peritoneal cavity. Death after this injury most often is due to associated injuries but ruptured diaphragm may

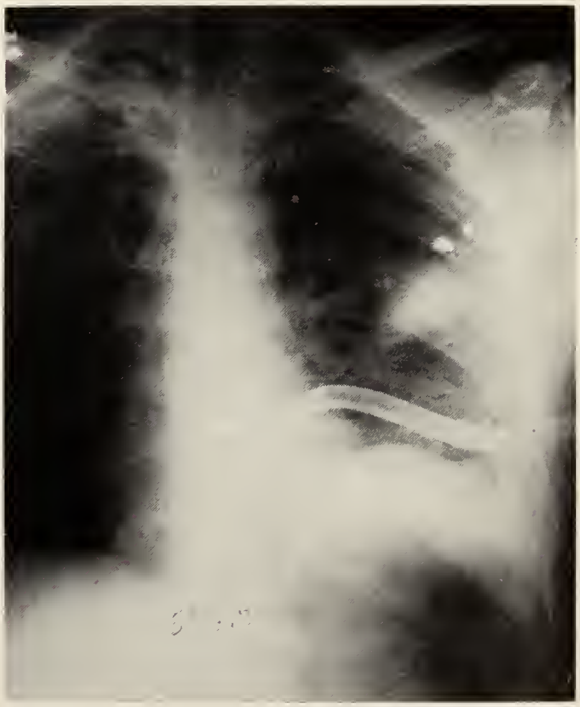

Fig. 8. Contusion of lung produced by gunshot wound. No tracheobronchial bleeding occurred. Air and blood in the chest were evacuated by chest tube. Recovery was uneventful.

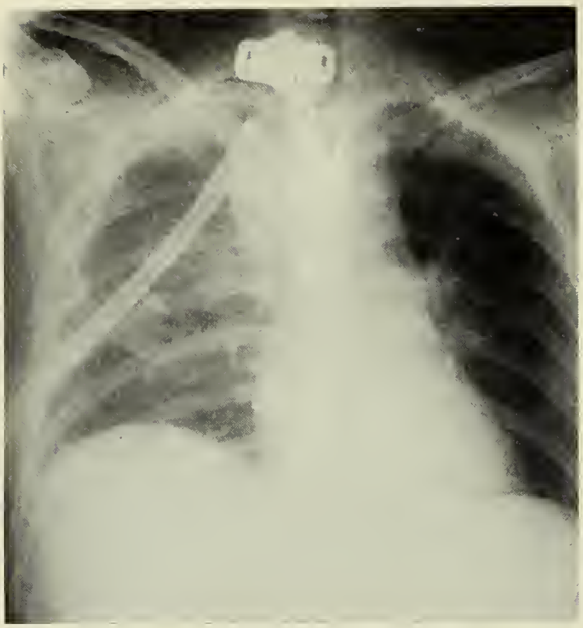

Fig. 9. Widening of superior mediastinal shadow due to mediastinal hematoma from laceration of innominate artery. Metallic device was used in an attempt to stabilize a flail segment of chest wall. The arterial injury was not recognized and exsanguination occurred.

lead to a fatal outcome if the diagnosis is missed and interference with the blood supply of the trapped viscera leads to gangrene.

Lung contusion. Contusion of the lung (Figs. 7 and 8) occurs after both penetrating and closed trauma. Rarely, contusion of the lungs may cause death because intraparenchymal hemorrhage is so extensive as to interfere with respiration; it is more likely to be lethal because of bleeding into the tracheobronchial tree. Tracheotomy and tracheobronchial lavage with normal saline and suction usually serve to keep the tracheobronchial tree clear until bleeding ceases. This may require constant attendance for a prolonged period. Operation is rarely indicated.

Laceration of great vessels or the heart. Bleeding into the pleural cavity may be severe and rapidly lethal or hemorrhage may be initially confined in the mediastinum. With free bleeding into the pleural space, the patient is usually in profound shock and unresponsive to resuscitative measures on hospital arrival and blood in the chest is demonstrated by thoracentesis. Immediate operation may avert a fatal termination. Two patients with such injuries seen in our hospital in the past two years have both survived following rapid diagnosis by house officers and thoracotomy. In the five-year period just before this time, patients with injuries of this nature died. Hemorrhage from great vessel injury confined to the mediastinum initially may produce death from blood loss later when rupture into the pleural cavity occurs. This injury may be apparent on the admission chest X-ray as widening of the mediastinum (Fig. 9). Diagnosis can be made by angiography if the injury is suspected. Treatment is immediate surgical repair of the injured vessel. Bleeding from injuries to the heart may be initially confined to the pericardium and the presenting symptoms may be due to pericardial tamponade. Pericardiocentesis under these circumstances is lifesaving. Most such injuries then require thoracotomy and suture of the heart wound for survival.

Rupture of bronchus or trachea. Rupture of intrathoracic trachea or bronchus should be suspected with mediastinal emphysema and pneumothorax, if reexpansion of the lung does not follow insertion of chest tubes and application of suction and if the air leak by that route is great. Diagnosis is confirmed by bronchoscopy and selective bronchography. Treatment is early surgical repair of injured bronchus or trachea.

Rupture of esophagus. Traumatic rupture of esophagus is more likely to occur following penetrating injury. Diagnosis will be suspected with mediastinal and cervical emphysema with or without pneumothorax and can be confirmed by esophagoscopy or esophagram. Treatment is surgical repair of damaged esophagus.

Chylothorax. Chylothorax from injury to the thoracic duct is a very uncommon injury. Diagnosis will be made if chest drainage contains chyle following a thoracic injury. Initial treatment is by chest drainage with tubes. If the condition persists, thoracotomy for ligation of the thoracic duct is necessary.

SUMMARY

Thoracic injuries are common and are often responsible for death of the patient with multiple injuries. They may be overlooked or treatment may be delayed while other more obvious derangements such as fractures receive attention. Since most severe thoracic injuries result in hemorrhage and interference with ventilation, they require early and vigorous treatment if the patient is to survive.

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Vertebral Column Injuries

MAX E. ZARLING, M.D.
St. Paul

VERTEBRAL INJURIES and associated nervous system injuries present problems in treatment as well as in diagnosis when they are noted singly. In the presence of multiple injuries, the diagnosis is often obscure and the treatment is often handicapped. Primary significance of vertebral fractures is injury of central nervous system function. Relief of injury, if present, prevention of acute deterioration, and lessening chance of late-developing injury are aims of therapy.

Time is important in the institution of treatment. Multiple injuries again complicate rapid diagnosis. The patient who is alert and has a history of subjective complaints, such as inability to move the extremities, numbness, or radicular pain, presents little problem in leading to pertinent diagnostic procedures, usually X-rays. However, in the patient who concomitantly has a head injury with a disturbed state of consciousness, as is too often found with an injury such as a car accident, multiple neurological defects are found. In the presence of a state less than coma, certain features may be valuable in suggesting an injury to the spinal cord and the nerves leading from it. There are two general features that are associated with all injuries to the spinal cord in the acute state. There is a total paralysis of all nervous system function below the level of the lesion which is commonly known as "spinal shock" and is characterized by a flaccid paralysis. The spasticity that is familiar in the paraplegic and quadriplegic patient does not develop for a period of two to three weeks, and often longer, following the injury. This state of spinal shock is present in injuries at all levels of the cord itself, although, below the level of the cauda equina, little motor dysfunction will be noted of the extremities. While flaccidity may be encountered with injuries of the brain, spasticity is never noted with a cord injury. Asymmetrical flaccidity is usually the result of a brain injury rather than a cord injury. The other general feature that is almost always noted is a flaccid paralysis of the bladder. This also will occur at all levels of cord injury, including the cauda equina. There are other characteristics of injuries at varying levels along the spinal axis.

DIAGNOSIS

Fractures or dislocations above the fourth cervical level and complete lesions are usually followed by rapid death. Probably the most common site of fracture in the upper cord is at the C1-2 level, with a fracture dislocation of the odontoid process. Fortunately, the region of the foramen magnum presents the greatest amount of room for a space-occupying mass, such as the odontoid process, so that the displacement may be present without evidence of cord abnormalities. If there is acute compression of the cord in this area, the usual result is death secondary to respiratory paralysis. Because of involvement of the muscles of respiratory function, injuries to segments above C4-5 also are often fatal. Occasionally, pain in the occipital scalp is found as evidence of a C1-2 injury.

Fractures at the C5-6, C6-7, and C7-T1 are the most commonly seen of cervical fracture dislocations. They may be the result of any acute flexion or extension type of injury, most commonly extension, but they also may result from injuries in the axis of the vertebral column, such as striking the buttocks forcibly, and also from lateral injuries. While the cord functional level at C5-6 corresponds approximately to the C7 level, usually cervical rootlet damage is sufficient to place a level with the sixth cervical nerve rootlet and, inferiorly, C7 and C8, respectively.

Injuries at the C5-6, therefore, present as inability to adduct and move at the shoulder level, with no movement of flexion or extension at the elbow or of the hands. Concomitantly, there is a lack of response to pain, generally below the midportion of the upper arm inferiorly. Similarly, there will be no response to axillary pain and response to pain only above the clavicles. Again, there would be a flaccid paralysis. In the semicomatose patient, when the arm held above the

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MAX E. ZARLING *is consultant in neurosurgery, St. Paul–Ramsey Hospital, St. Paul.*

patient's face is dropped, the hand will strike the face, but the shoulder will generally carry the arm off laterally. In the semicomatose patient, pain responses can usually be elicited in one nature or the other, but only from the upper arm and lower neck and face. If any pain response is found distal to this, particularly in the lower extremities and even if completely flaccid, an incomplete lesion may be presumed. A physiological sympathectomy is found bilaterally with a lesion above the first thoracic nerve roots which form the exit of the sympathetic nerves. This often is accompanied by warm, dry skin, later followed by pallor and coldness. There may be sweating above a definite level of the clavicles with no perspiration noted distally. Hypotension is often present and may complicate the problem of evaluating hemorrhage into the abdomen or elsewhere in the body. Priapism, if present, always is indicative of a spinal cord injury, although it may be incomplete. Respirations are generally impaired and primarily abdominal in nature. Ileus, associated with vomiting and, in turn, aspiration, also is often present.

Injuries at C6-7 are characterized by ability to flex the elbow, with loss of extension of the elbow and hand and finger movements other than wrist flexion. C7-T1 injuries primarily interrupt movements of the fingers with preservation of wrist and arm movements. At the C6-7 levels, sensation will be apparent through most of the upper extremity with the exception of the medial hand and arm, and at the C7-T1 level, less sensory loss of the upper extremity will be apparent with, perhaps, even good sensation of the entire hand. Again, both of these lesions are usually associated with a quadriplegia of the lower extremities of a flaccid nature, the absence of perspiration, ileus, and bladder function. In the comatose patient, the diagnosis will often be difficult, particularly for sensory level, if there is a lack of responsiveness, although, again, a flaccid paralysis suggests a cord lesion as well as the brain lesion which obviously is present already.

Injuries to the thoracic spinal cord are not common above the T11 level. These present primarily as a paraplegia with varying degrees of sensory loss, depending on the level of the fracture. Generally speaking, as far as sensory loss is concerned, the anatomical level implicates an injury 2 vertebral segments above. Flaccid paralysis is present, ileus is generally found, the bladder is nonfunctioning, and a sweat level is present also. Fractures at the lower thoracic and thoracolumbar junction and associated nervous system injuries are characterized by a paralysis of the varying portions of the lower extremities that may be secondary to cord injury and, also, to the peripheral nerve roots as they pass through the distal canal as the cauda equina. The common fracture at T12-L1 or L1-L2 has a sensory deficit at L1 or below because of injury to the cauda equina. Fractures of the lumbar vertebrae, with associated dislocations or even herniation of the intervertebral disks, acutely involve various muscle groups of the lower extremities with preservation of movements of the thigh below L1, presence of both flexion of the knee and movement of the thigh below L2-3, and extension of the knee possible below L3-4. L4-5 and L5-S1 injuries find paralysis of the feet alone. Fracture dislocations are rare, and prolapse of the intervertebral disk causing compression is more likely. Corresponding sensory levels along the lower extremities vary with the vertebrae involved, for example, anesthesia below the upper thigh with L2-3, below the lower thigh at L3-4, the medial foot and great toe with L4-5, and the lateral foot with L5-S1. Of course, associated with these is sensory loss in the saddle distribution.

Tendon reflexes are absent in the presence of a flaccid paralysis, and there is a loss of the biceps reflex and all those distal to it with a C5-6 fracture. The biceps reflex is preserved and the triceps reflex is absent with a C6-7 fracture. Similarly, the knee reflex is lost with an injury above L4-4 and the ankle reflex is lost above a level of L5-S1. The Babinski signs are absent, or a vermiform reflex is noted, particularly in total lesions. This is characterized by a slow plantar flexion of the great toe and a slow sequential flexion of the second to fourth toes, a grave prognostic sign.

TREATMENT

Diagnosis of fracture and dislocation, or both, is made by the X-ray. In the patient who has been in a car accident or who has multiple injuries, complete X-ray evaluation of the spine is ideal, although often impractical. Cervical spine X-rays should always be done on the patient who has had a head injury. Lateral and anteroposterior films are necessary, and, while the odontoid process is usually seen well enough in the lateral X-ray of the head, the open-mouth view can be of value also. Dislocation of the odontoid process can cause acute demise with movements such as sitting up. This, while rare, is doubly tragic because of the infrequency of permanent injuries secondary to a treated odontoid lesion. Because of the possibility of cervical spine fractures with head injuries, it is best to take across-the-table X-rays of the skull without manipulation of the head or rotation of the head, as is the usual procedure for elective X-rays, and to compromise with a single anteroposterior view of the skull. The open-mouth view, of course, may be used; in the acute situation, this will often suffice. Similarly, if thoracic or lumbar spine X-rays are considered, films are best if taken with the patient maintained in a single, supine position. A particular problem is the suspected lesion in the lower cervical or upper thoracic spine in a person with a short, thick neck. Oftentimes, pulling down the hands will provide adequate visualization, particularly at the C6-7 level. If this is not adequate, it may be necessary to elevate one shoulder slightly while moving the head in a corresponding angle of rotation and taking a picture with the film outside the other shoulder. Occasionally, tomograms are necessary.

Generally speaking, the serious lesion in the cervical spine will be of an anteroposterior dislocation rather than lateral, although this may be present, particularly with the crushing of a facet. In the thoracic region, it may be either lateral or anteroposterior dislocation and, similarly, in the lumbar region. Compression fractures are found most often in the thoracic and lumbar regions, and, while displacement may not be marked, this may be associated with protrusion of the intervertebral disks. While in the presence of a dislocation of the cervical spine no laminar fractures are obvious, still these are almost invariably present. Treatment of vertebral injuries actually is instituted with the suspicion of a lesion. This entails the maintenance of immobilization in transporting the patient and in diagnostic procedures. Immobilization can almost always be done in the supine position without necessity for manipulative positioning such as lumbar roll. Maintenance of the head in the neutral position with the use of sandbags is most practical until evidence of a fracture is proved or disproved.

Sound emergency treatment and catheterization of the injured patient also are definitely necessary in the patient with spinal cord injury. Hypotension associated with cervical cord injuries usually is not a type to compromise circulation. Respiratory dysfunction is the most common early cause of death in patients with cord injuries, particularly the cervical cord and especially in the presence of aspiration. Tracheostomy is often a lifesaving procedure in the quadriplegic patient, even without aspiration. Because of the ileus, gastric decompression is often necessary, even if not for a prolonged period of time. In general, the surgical emergencies that are seen, such as pelvic fractures with hemorrhage, intra-abdominal hemorrhage and viscus ruptures, and lung and cardiac injuries can be treated by recognizing that a state of immobilization is preferred. Endotracheal anesthesia, if necessary, should be done without movements of the neck, if possible, or by means of a tracheostomy. Necessary operations, other than those in the supine position, fortunately are rare and generally will not complicate the situation in the acute phase. Hemorrhage and respiratory dysfunction must be treated first, and cord injuries and fracture dislocations will probably follow next, with the possible exception of injuries to the brain. Orthopedic procedures generally can be deferred also.

Therapeutic immobilization of fractures in the cervical spine is best accomplished after the initial diagnostic procedures have been done. Head-halter traction, with canvas bands beneath the chin and the occiput of the head attached to a spreading bar and pulley and weights, usually is satisfactory, with the possible exception of the presence of multiple facial bone injuries. Traction weights will vary with the size of an individual and an adult male will tolerate 8 to 12 lb. for a period of hours or even days. Children will take a lesser amount of weight. The best means of traction for the cervical region is skeletal traction; Crutchfield tongs or other skeletal traction devices can be used. Under local anesthetic, these are easily inserted in the scalp and are well tolerated once the patient is reassured of his relative comfort in comparison with halter traction. Skeletal traction apparatus, consisting of tongs and a small bit that inserts in any hand drill, are a valuable addition to all hospital operating room equipment. Traction in the axis of the neck is most satisfactory without attempts at flexion or extension. While the principle of immobilization is of primary consideration, secondary reduction of fracture dislocations is readily performed with traction of varying weights. With thoracic vertebral fractures, reduction is not possible, and decompression of the lamina is the preferred treatment with a severe dislocation. Similarly, in the lumbar region, a lordotic roll reduction may be tried, but often decompression is the only effective treatment. Pelvic traction is of little use.

Manipulation of vertebral fractures, with or without anesthesia, has no place in the treatment of these injuries. Extra caution must be exercised if operative procedures are necessary with general anesthesia, because of relaxed muscles and danger of easy dislocation or redislocation.

No cervical fracture dislocations should be treated without an attempt at restoration of normal skeletal position, even though neurological deficit is not present acutely. Fractures of the odontoid are notoriously unstable. Healing across the break at the base of the odontoid is rare because of lack of blood supply. Prolonged immobilization in either skeletal traction or some type of bracing or a fusion of the upper two or three cervical vertebrae is usually necessary. A fracture dislocation of the remainder of the cervical spine after reduction may be maintained in traction for six weeks, with a three- to six-month period of bracing before it is considered stable. Fractures and dislocations of the thoracic and lumbar spine not entailing neurological deficit may be treated by immobilization for the period of symptoms and bracing for up to six months.

There are many opinions regarding surgical management of fracture dislocations of vertebrae. Procedures encompass minimally a decompressive laminectomy. In certain situations operation is definitely indicated. A compound injury to the spinal cord or evidence of bony fragments impinging upon the spinal canal indicates the necessity for removal of these foreign bodies. If a lesion is progressive, need for surgery is obvious. Inability to reduce the skeletal lesion, even though neurological deficit is not significant, generally indicates a combination reduction and decompression procedure. The greatest decision is what to do for the patient with complete loss of function secondary to fracture, regardless of the level at which it occurs. Some suggest that with an acute complete lesion prognosis for recovery is so slight that operative interference is never indicated. Others hold that all complete lesions should have emergency operations for decompression based upon experimental results that decompressing a cord within two hours can result in recovery of partial, if not complete, function.[1] Often, decompressive laminectomy is done largely for psychological reasons. The feeling is that the patient and his family are better able to accept the injury if they know that everything possible has been done. A lumbar puncture and Queckenstedt's test to demonstrate the presence of a spinal fluid block are used by some in the decision to undertake surgery.[2]

In the presence of an incomplete lesion, immediate operative interference again is seldom indicated unless foreign bodies are present within the spinal canal or the bony deformity is impossible to reduce. However, this is not an acute situation and traction reduction, particularly to the cervical spine, often can be accomplished over a period of several days. In regard to the decompression, some surgeons consider procedures complete only with the opening of the dura and section of the dentate ligaments,[3] but others feel that incising the dura may cause further injury to the cord with extrusion of the cord contents. Anterior cervical fusion,[4] when done in the presence of a complete lesion, is generally for the purpose of early ambulation of the patient. Often the patient may be out of bed within a week or two and able to begin physical therapy much earlier than with traction or immobilization. Fusion of injuries below the cervical region is usually done later. Traction is maintained during all operations of the cervical spine; local anesthetic is sometimes used but generally endothracheal anesthesia is necessary.

DISCUSSION

Generally prognosis in acute complete lesions at all levels is poor,[5] although some recovery can occur in a period of weeks or months, particularly in lumbar spine injuries. Lumbar spine injury is primarily to peripheral nerves, and there is certainly a greater chance of recovery than with cord injury. While morbidity in incomplete lesions is high, there is reason for optimism for return of function. In patients with an acute incomplete injury, repeated examinations are important. These can be performed by the nursing staff and include such things as ability to move the extremities and to perceive sensation. Neurological function in spinal cord injuries should be followed as closely as in head injuries, for example, at hourly intervals. The forty-eight-hour period following the injury is the most critical as far as progression of symptoms is concerned, although further changes may be noted over several days. In an acute lesion, if surgery appears desirable, there would seem to be less purpose in emergency operation except within the first several hours after the injury.

SUMMARY

Diagnosis of vertebral fractures is sometimes difficult and treatment is often unsatisfactory. However, in some situations further injury may be prevented. Success depends upon the diagnosis, proper emergency management, and recognition that surgery is of benefit at times.

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Initial Treatment of Pelvic Fractures

CHARLES W. HAUSER, M.D.

St. Paul

FRACTURES OF THE PELVIS have been shown to be a leading cause of death in victims of traffic accidents and, especially, of pedestrians struck by vehicles.[1] For this reason, all persons who have sustained significant trauma from any cause should be evaluated for pelvic fracture at the time of admission to the emergency room. Fractures of the pelvis should not be overlooked because of other significant injuries.

The most common, and by far the most serious, complication of pelvic fracture is hemorrhage. An analysis of our experience with 196 patients with pelvic fractures over a recent five-year period revealed that one-third of these patients required blood transfusion because of hemorrhage from the pelvic fracture.[2] Of 15 patients who died primarily as a result of fracture of the pelvis, the cause of death was massive hemorrhage in 9, fat embolism in 2, arteriosclerotic heart disease in 2, and severe ileus with electrolyte imbalance in 2.

McCarroll's group[3] and Peltier[4] emphasized that patients dying of intrapelvic hemorrhage have a relatively long survival period which affords time for an orderly and effective program of blood replacement. This has not been our experience, however, as two-thirds of our patients succumbing of hemorrhage from pelvic fractures died within four hours of admission to the receiving room. For this reason, we have developed a very aggressive approach of blood replacement and efforts to control blood loss, as will be described later.

As would be expected, the more extensive the pelvic fracture, the more likely is massive hemorrhage to occur. In this regard, the roentgenogram of the pelvis can be helpful in predicting which patient will need extensive blood replacement. On the other hand, one should remember that even a slightly displaced fracture of a single pubic ramus will occasionally cause hemorrhage severe enough to result in hypovolemic shock.

Of our patients with a double break in the pelvic ring or more extensive fractures, two-thirds required transfusion, each receiving an average of 7.4 units of blood, and 20% died primarily as a result of pelvic fracture. In contrast, of the remaining patients with lesser degrees of pelvic fracture, approximately 30% required transfusions with an average of 1 unit of blood each, and the mortality rate from the pelvic injury was only 4%. The least serious fracture was found to be isolated fracture of the acetabulum followed by isolated fracture of the wing of the ilium and fracture of a single pubic ramus. This agrees with the findings of Peltier.[4]

The next most frequent complication of pelvic fracture is injury to the bladder or urethra, or both. This occurred in 8% of our patients as compared with 10% reported by Peltier. The diagnosis of bladder and urethral injuries is usually relatively simple. If a patient is suspected of having such an injury either because of the nature of the pelvic fracture, hematuria, or symptoms, an indwelling catheter is inserted, if possible, and a cystogram is obtained. If the bladder and urethra seem intact and hematuria persists, an intravenous pyelogram is obtained. The treatment of these injuries is discussed in a separate article by Hakim.

Less frequent complications of pelvic fracture are fat embolism and ileus, both usually being manifest a day or more after the injury, although effects of fat embolism can be apparent on occasion from the time of admission to the hospital. A discussion of the methods of recognition and treatment of these conditions is not within the scope of this paper.

Rare complications of pelvic trauma are injuries to the rectum, vagina, uterus, adnexa, and lumbosacral nerves. None of these were encountered in our experience.

Associated injuries are common in patients with fractures of the pelvis because of the nature of injury. The most frequent associated injury is fracture of one lower extremity, followed in order by injury to the chest, fracture of the up-

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CHARLES W. HAUSER *is from the department of surgery, St. Paul–Ramsey Hospital, St. Paul.*

per extremity, and head injury. Also commonly involved are the abdominal viscera, especially the spleen and liver.

It is extremely important to differentiate between intra-abdominal hemorrhage from injury to the abdominal viscera and hemorrhage from pelvic fracture. Blood loss from each is occult, but to treat hemorrhage from an intra-abdominal organ nonoperatively can be a fatal error while the usual treatment of intrapelvic hemorrhage is simply blood replacement. For this reason, in any patient with occult blood loss and the least suspicion of having an intra-abdominal injury, we do a diagnostic peritoneal lavage as described by Root and associates.[5] If this test is positive, exploratory laparotomy is performed; if negative, nonoperative management is instituted unless massive hemorrhage from the pelvis persists. We wish to stress that massive, exsanguinating hemorrhage from pelvic fractures can be, and frequently is, confined to the retroperitoneal space and there need be no free blood in the peritoneal cavity in such cases.

Movement of patients with pelvic fractures should be avoided as this is likely to lead to further hemorrhage. All patients at our hospital suspected of having sustained a pelvic fracture are transferred from the ambulance stretcher to a firm, padded board, as described by Root.[6] By keeping a patient on this firm support until his condition is perfectly stable, further movement for obtaining roentgenograms, for transfer to bed, and so on, is eliminated. We feel that this is adequate immobilization for any pelvic fracture in the initial acute phase following injury and is preferable to any type of sling support which requires movement of the patient to apply.

Just as in any of our traumatized patients presenting with hypotension, patients with pelvic fractures are transfused with O negative blood (until cross-matched blood is available) if they remain hypotensive after receiving 500 ml. of lactated Ringer's solution intravenously over five or ten minutes. Any patient admitted in profound shock following trauma is given blood immediately. Blood transfusions are continued as rapidly as necessary until blood pressure has been restored. If shock persists or recurs despite rigorous replacement, and all other causes of massive hemorrhage have been ruled out, we feel that ligation of the hypogastric artery on the more involved side should be performed. Following this, if hemorrhage is not abruptly controlled, the other hypogastric artery should also be ligated. Our experience utilizing this technique in 4 patients has been reported previously.[7]

We feel that ligation of the hypogastric arteries to control massive hemorrhage from pelvic fractures can be a lifesaving procedure and is relatively simple to perform. Complications secondary to this procedure have not been reported, although it would be contraindicated in patients with preexisting occlusive disease of the external iliac arteries. Nevertheless, it should be made clear that relatively infrequently is it necessary to resort to this procedure in the treatment of hemorrhage from pelvic fractures. More often, massive hemorrhage responds very well to vigorous blood replacement initially with only a few transfusions required thereafter.

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Trauma to the Female Genitalia

ERICK Y. HAKANSON, M.D.

St. Paul

NONSURGICAL and nonobstetric injuries to the female reproductive organs have not been reported frequently in medical literature. These wounds are either of the penetrating type, such as gunshot or knife wounds, or due to blunt trauma such as automobile accidents. Independently in 1954, Kobach and Hurwitz[1] and Wright and associates[2] collected between them 41 case reports of perforating wounds to the gravid uterus from the world's literature since 1845. Quast and Jordan[3] in 1964 collected 13 additional cases of perforating wounds to the uterus and reported the experience of 2 general hospitals over a fifteen-year period. Their case reports included 16 gunshot wounds, 7 stab injuries, and 4 blunt trauma. Ten of their patients were pregnant. In 1936 Lazard and Kliman[4] reviewed 41 cases of nonpenetrating wounds reported in the literature through 1936 and added 1 of their own. Since that time there have been sporadic case reports of blunt trauma to the pregnant uterus.[5-11] Generally, obstetric reviews of rupture of the uterus do not include cases of nonobstetric or nonsurgical etiology.

If injuries from attempted or actual criminal abortion are excluded, the mortality from trauma to the internal and external genitalia per se must be very small. Barno, Freeman, and Baken[12,13] have reviewed the ten-year experience of the Minnesota Maternal Mortality Committee. This report, from the period 1954 to 1964, covers approximately 819,180 births. During that period 203 pregnant patients lost their lives from nonobstetric causes. The most frequent cause of death was trauma, which was responsible for 33 deaths. Seventeen (52%) were due to auto accidents, 9 (27%) were due to suicides, 4 (2%) were homicides, 2 resulted from accidental drowning, and 1 was from burns. Only 1 of these deaths was exclusively and directly related to injury to the pregnant uterus. This case will be discussed later. In the report of Quast and Jordan cited above, only 1 patient died and that death was the result of other associated injuries.

Although these reports indicate that injuries to the female organs are rare and are in themselves associated with an extremely low mortality, there are a number of other considerations which may indicate that these injuries are a unique and important medical and surgical problem. While in the normal state the female genitalia are well protected, this situation is changed with respect to any enlargement and makes the pregnant uterus especially vulnerable to injury. In addition, since the preservation of life is the first consideration in any management of acute injuries, this goal becomes doubly important in the case of the injured pregnant patient. Lastly, the preservation of the reproductive function is likely to be the most important consideration to the young female patient with injuries to her genitalia.

The present report deals only with injuries to the internal and external genitalia that were serious enough to warrant admission to the hospital. These injuries were not related to surgical or obstetrical trauma and complications, or both. Also, all injuries as a result of attempted or actual criminal abortion were excluded. The time period of this report covers 101,022 admissions from Jan. 1, 1956, through Dec. 21, 1965.

Table 1 gives the number and distribution of genital injuries.

TABLE 1

Perineum and vulva	3
Vagina	19
Cervix	1
Uterus, nonpregnant	0
Tube	0
Uterus, pregnant	4
Ovary	0
Multiple	2

Injuries to the vulva and perineum usually involve falling with considerable force on a sharp

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ERICK Y. HAKANSON *is head, Department of Obstetrics and Gynecology, St. Paul–Ramsey Hospital, St. Paul.*

object or edge. All of the above 3 cases involved such injury with resulting huge hematomata. While hypovolemic shock did not occur, significant drops in hemoglobin occurred in all cases. These patients were all treated with incision and drainage as soon as practicable after admission. They all recovered quickly without infection. No prophylactic antibiotics were used. On the basis of our experience, if the hematoma is circumscribed enough to be drained, this procedure should be done both to lessen the pain and also to speed recovery and prevent secondary infection. As in any other widespread hematoma, a careful family and personal history to rule out bleeding defects should be taken.

One other patient sustained a shotgun injury at close range. This discharge resulted in the entire left side of the vulva, introitus, perineum, and part of the lateral distal vagina being completely blown off, with considerable loss of subcutaneous tissue. Miraculously, the urethra, bladder, rectum, and major vessels remained intact. This accident occurred in an 11-year-old girl. Blood loss was not alarming, and initially only thorough cleansing and debridement was carried out. She did not become infected and quickly regenerated her tissues. Because of the injury to the introitus, a small lucite mold was placed in the vagina to prevent closure from scarring. Examination one year later revealed very little evidence of her injury other than some loss of subcutaneous tissue over the symphysis on the side of her injury. This area remained tender to deep palpation. It is the experience of obstetricians and gynecologists that the skin of the perineum and vulva has a truly remarkable capacity to regenerate and heal itself.

The 1 instance of injury to the cervix was unexplained. The patient was not pregnant. She was a 28-year-old para 2-0-0-2 who came in with acute vaginal bleeding. Examination revealed a laceration at 9 o'clock, deep. She denied the possibility of any foreign objects being placed intentionally or unintentionally in the vagina. It was repaired under general anesthesia. Blood loss required 2 units of replacement. One surgical consideration in laceration of the cervix is the possibility of involving the ureters in any deep sutures placed in the lateral fornices and paracervical area. In cases of very deep and extensive lacerations here, either ureteral catheterization or direct visualization of the ureters would be indicated.

There were 19 vaginal lacerations admitted. Undoubtedly, some of these could have been treated on an outpatient basis. However, all of the above cases showed significant drops in hemoglobin and 2 were in frank hypovolemic shock. Sixteen were single lacerations and 3 were multiple. Fourteen involved the posterior half of the vagina. Only 1 involved the urethral meatus. None involved rectum or cul-de-sac perforation. An interesting feature of these lesions is that the etiology remains difficult to prove. It seems reasonable that sexual relations can cause vaginal lacerations, especially in the immediate postpartum period. Eight of the patients stated that vaginal bleeding, sometimes described as violent, started during or shortly after intercourse. Of the remaining 11, 2 admitted that a foreign object had been placed in their vagina before the onset of bleeding. The remaining 9, including the 2 patients in shock, would not admit to any causally related circumstance. It seems likely that a considerable number of vaginal lacerations are caused by foreign bodies. In the case of multiple severe lacerations, it should be assumed that the etiology is the latter and a careful search for remnants of foreign bodies such as glass or metal should be made, together with an AP and lateral X-ray to include the vagina. Obviously, perforation of the rectum, cul-de-sac, bladder, and urethra must be ruled out. To avoid shortening and contraction of the vaginal mucosa, sutures of chromic 0, 00, or 000, mostly in interrupted fashion, were used to unite mucosal edges. All healed without complication or significant febrile course. Prophylactic antibiotics were not used.

The other multiple injury was that of a 5-year-old child who sat down hard on an old-fashioned, long, pointed phonograph spindle. In addition to the pain, she began to pass blood tinged urine. She was admitted to the urology service where she continued to pass blood in the urine overnight. Cystoscopy did not reveal the source of the bleeding. Gynecological examination was remarkable in that there was no external evidence of trauma. However, careful inspection of the vagina under anesthesia revealed a small perforation of the posterior vagina and another one in the anterior vagina at a deeper level. Anoscopic examination confirmed the suspicion that the spindle had entered the anal opening, perforated the rectovaginal septum, continued through the vagina, and at least partially entered the bladder. Although technically difficult because of lack of exposure, both perforations were closed in layers with intestinal chromic 00. The patient recovered uneventfully. Seven years later she had to have a hematocolpos incised because of an imperforate introitus, undoubtedly due to the trauma of the above surgery. In retrospect, the introitus should have been kept open either by a tiny mold or by periodic dilation.

Four injuries to the pregnant uterus were recorded.

CASE REPORTS

Case 1, a 33-year-old para 2-0-0-2, accidentally shot herself with a .22-caliber rifle at close range at approximately twenty-six weeks' gestation. No fetal heart tones were heard on admission, although the patient stated she had felt life up to the time of the accident. A flat plate of the abdomen revealed the bullet to be located near the acetabulum of the left hip. She was not in shock. Exploratory celiotomy revealed 300 to 400 cc. of blood. The entire small and large bowel were inspected and no areas of perforations were found. A wound of entrance in the uterus was found about 3 cm. to the right of the midline just below the insertion of the round ligament, apparently making its exit on the lower left side of the uterus without perforating the serosa, and continued laterally out the broad ligament and retroperitoneally toward its resting place near the left acetabulum. There was a small hematoma in the left broad ligament. There was no active bleeding and the uterus was not firm. The areas of perforation were closed with figure of 8 chromic 0 catgut. After inspection of the bowel, the abdominal cavity was washed well and closed. No fetal heart tones were heard during the postoperative period. Ten days later the patient spontaneously delivered a 465 gm. macerated infant with no gross anomalies. There appeared to be a bullet wound of entrance in the postaxillary line on the left and an oblique wound in the anterior abdomen measuring 2 × 6 cm. from which multiple loops of small bowel protruded. The placenta was still attached. The major vessels were intact. The mother recovered without complications.

Case 2 was a 22-year-old para 1-0-0-1 who, at twenty-three weeks' gestation, was shot with a .22-caliber rifle by a deranged husband from a distance of about 20 ft. Although she was in clinical shock when first seen, the fetal heart tones were audible and regular. Exploratory celiotomy revealed multiple perforations of the small bowel with hemorrhage. There were 2 small areas of perforation at the top of the fundus, 1 anterior and 1 posterior. The anterior was about 3 cm. below the posterior. The path of the bullet was superficial enough to be visible. There was minimal bleeding. It was not probed for fear of causing bleeding, and simple figure of X catgut sutures were placed at each perforation. In spite of a stormy postoperative course due to complications of bowel surgery, she delivered an apparently normal 6 lb. 12 oz. infant spontaneously at thirty-eight weeks without complication. External and internal palpation of the uterus revealed no defects.

Case 3, a 29-year-old para 1-0-0-1, who at thirty-eight weeks' gestation was involved in a head-on automobile collision, was brought to the emergency room with no blood pressure obtainable. With bilateral cutdown and pumping of 3 units of whole blood, the blood pressure was brought up to 80 to 90 mm. Hg. She had apparently sustained a crushing injury to the upper abdomen and chest from the steering wheel. The patient was disoriented and agitated. She began to bleed profusely into subcutaneous tissue of the neck and breasts and from soft tissue lacerations of the face. The uterus was intermittently contracting. She was 4 cm. dilated with membranes intact. Fetal heart tones could not be definitely ruled out since the maternal pulse was 140 to 160. She bled also from venipuncture sites. Consequently, a sample of venous blood was drawn which did not clot. She was given 4 gm. of fibrinogen (all that was available at that time) in addition to 3 more units of whole blood. She was moved to the operating room for the purpose of doing a tracheostomy because of increasing respiratory distress. Her systolic pressure was 60 to 80 mm. Hg. Shortly after institution of suction and intermittent positive ventilation, no cardiac sounds were heard. Attempts at closed resuscitation were unsuccessful. One team quickly removed the baby from the uterus. It was a grossly normal 3,730 gm. male. The placenta was completely separated and there was free blood in the uterus. An area of contusion of the lower posterior portion of the uterus was noted. The other team tried open chest resuscitation without success. Postmortem diagnoses of the mother were: (1) multiple rib fractures with bilateral hemothorax and massive bleeding in the anterior chest wall and breasts, (2) left lung atelectasis, (3) multiple soft tissue injuries, (4) petechial hemorrhage, right cerebral hemisphere, and (5) thirty-eight weeks' gestation with evacuation by means of classical uterine incision.

Postmortem diagnosis of the infant was: stillborn male infant, intrauterine anoxia, clinical.

Case 4, a 22-year-old primipara, was involved in an automobile accident three days past her expected date of confinement. She had had a normal prenatal course. She was thrown free of the car and apparently landed on her abdomen. She was brought quickly to the emergency room where her blood pressure was originally 130/70 mm. Hg but decreased to 90/55 mm. Hg during the next hour. She was awake and responsive. She had many contusions and superficial lacerations but no apparent head injury or broken bones. The abdomen was tender and became more so. She began to have vaginal bleeding. The uterus became increasingly firm. Fetal heart tones were absent. A diagnosis of abruptio placentae was made and the membranes were ruptured. Since labor did not begin, dilute Oxytocin drip (Pitocin®) was started and after six hours she delivered a 3,720 gm. stillborn infant and placenta with large clots attached. She received 4 units of blood during and after delivery. Clotting defect was not investigated.

As was mentioned previously, there was 1 maternal death in the Minnesota Maternal Mortality ten-year review. This patient was involved in an automobile accident at thirty-nine weeks' gestation. Since she was able to walk into the emergency room one-half hour after the accident, attention was directed to the other occupants who were thought to be more seriously injured. She had a fair amount of vaginal bleeding. About one-half hour later she was found to be sitting up in profound shock. After being placed in the Trendelenburg position, she awoke and complained of abdominal pain, backache, and continued vaginal bleeding. In spite of emergency measures and somewhat delayed blood transfusion, the patient died two and one-half hours after admission. Autopsy revealed 2,000 cc. of blood in the peritoneal cavity and Couvelaire uterus and a broad ligament hematoma. There was a posterior laceration of the lower uterine segment measuring 2½ in. The placenta was completely separated. There were no other intra-abdominal lacerations or perforations. This death occurred before the relationship of afibrinogenemia to abruptio placentae was generally recognized, and no observations were recorded regarding the coagulability of this patient's blood.

DISCUSSION

There are a number of points that need to be emphasized with respect to both the diagnoses and management of injury to the pregnant uterus. As to diagnosis, it is important to establish whether (1) the uterus is intact, (2) there is any hemoperitoneum, (3) any premature separation of the placenta has occurred, (4) the blood has normal coagulability, and (5) the fetus is dead or alive.

In the case of perforating wounds of the abdomen, exploration is indicated in all cases so that intactness of the uterus can be established at that time. In nonpenetrating injuries, the integrity of the uterus must be established indirectly by means of colpotomy or culdotomy to rule out fresh blood in the cul-de-sac. If the cul-de-sac is scarred down from previous disease or injury, the abdominal approach as described elsewhere in this text can be used. While hemoperitoneum usually causes symptoms, its development can be at times insidious and its symptoms minimal. Rupture of the spleen or lacerations of the uterus can exist with minimal symptomatology initially. A positive colpotomy means exploration. Simple AP and lateral X-rays have revealed the fetus lying outside of the uterus in otherwise unsuspected rupture of the uterus.[10]

Although trauma causes only 1 to 2% of all cases of abruptio placentae, premature separation can be expected in a majority of severe blunt injuries to the pregnant uterus.[9,10,14] It should be remembered that shock itself can be considered a factor in the etiology of premature separation, especially in the hypertensive patient. Abruption due to trauma produces the same clinical picture as abruption due to other causes. However, it is likely to be complete and may be associated with laceration of the uterus or hemoperitoneum from other causes. If the abdomen is opened for other reasons, the presence or absence of hemorrhage of the uterine wall should be noted, as well as the tone of the uterus itself.

Because of the association of afibrinogenemia with abruptio, it is imperative that the competence of the clotting mechanism be established immediately and continually. Practically, this can for clinical purposes be established by drawing venous blood carefully into a clean tube, taping it on the wall, noting the time, and watching for the time of good clotting and how well the clot maintains itself. This procedure should be repeated at half-hour intervals. Obviously, an adequate amount of fibrinogen (9 gm.) should be easily available for treatment.

Management of injuries to the pregnant uterus must recognize many factors. These include: (1) stage of gestation, (2) age and parity, (3) extent of the injury, (4) condition of the fetus, (5) the seriousness of the associated injuries, and (6) the presence of premature separation and hypofibrinogenemia. Space does not permit an examination of each of these factors. Nevertheless, certain general principles should be emphasized.

While the maternal mortality is undoubtedly low, no accurate estimate can be given because of the paucity of reported cases. The fetal outcome is uniformly poor in gestations less than twenty weeks. In viable pregnancies, the outcome for the child is likely to be determined largely by the type and extent of the injury rather than by the treatment per se. Kobak and Hurwitz[1] reported a 55% mortality rate in their review of penetrating injuries. The fetal mortality from blunt trauma may be even higher.

A review of the recently reported cases strongly supports the conclusion that conservative management offers the best chance for survival of both mother and child. That is to say, all efforts should be directed toward preserving the pregnancy and allowing it to continue to term and delivering normally from below. There is little justification for removing the fetus simply because the uterus is lacerated. Many reported cases have documented the fact that the lacerated uterus can be repaired and heals well. Even in cases of extensive damage to the uterus and prematurity of the infant, it may be prudent to repair the lacerations as a first step, and later, under more optimal conditions, to do an elective cesarean section. Likewise, emergency hysterectomy is rarely necessary except in instances of a hopelessly lacerated uterus or in hemorrhage uncontrollable by other means. In the young patient without children, all possibilities should be exhausted in order to preserve the reproductive function intact.

It should be emphasized that associated injuries are present in approximately 70% of injuries to the pregnant uterus and, more often than not, are more immediately life threatening. This fact again supports the thesis that obstetrical management should be as conservative and supportive as possible so as not to complicate the management of the other injuries.

In cases of suspected or actual abruption, the management should be directed toward the prevention of excessive blood loss and the development of the clotting defect, or both. The usual indication for cesarean section in premature separation can safely be used, bearing in mind that the goal nonetheless is a spontaneous vaginal delivery.

There are many other aspects to the general problem of these interesting injuries, such as the precautions to be taken for all pregnant women undergoing emergency surgery for other reasons, as well as the problem of the damaged infant without damage to the uterus.[15]

Because of the multiplicity of factors, obstetrical consulation is recommended in all cases of significant genital injury. Lastly, because of the scarcity of well documented cases in the literature, more of these interesting lesions should be reported.

SUMMARY

Twenty-nine cases of injury to the female genitalia are reported, together with a review of previously reported cases.

The pregnant uterus is the most commonly injured organ, according to the literature.

Injuries to the pregnant uterus present multiple diagnostic and therapeutic problems.

A recommendation was made for conservative management in most cases, reserving cesarean section for well recognized indications.

Obstetrical consultation is suggested for all cases of injury to the pregnant uterus.

More reporting of these cases is urged.

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Trauma to the Urinary Tract

A. A. HAKIM, M.D., and
NASSER JAVADPOUR, M.D.

St. Paul, Minnesota

THERE ARE 2 main causes of trauma to the urinary tract: [1] external violence (accidents, falls, gunshot wounds, and so forth) and [2] injuries resulting from surgical and obstetrical procedures. The incidence of trauma to the urinary tract has increased over the past twenty years, mainly due to the increase in traffic and industrial accidents. Such accidents often cause concomitant injuries to the intraperitoneal viscera and severe bone fractures, and these usually pose more of an immediate threat to the patient's life than any injury to the urinary tract per se.[1,2] Nonetheless, an injury to the urinary tract may be fatal if not recognized early and treated adequately.

DIAGNOSIS

Immediate recognition and proper management of the injury are of paramount importance. The reduction in mortality depends upon three main factors:[3] [1] adequate treatment of shock and hemorrhage, [2] early and accurate diagnosis, and [3] proper management of other accompanying injuries (for example, immobilization of fractured bones).

After shock and hemorrhage have been dealt with, the diagnostic investigation should begin with an examination of the site of injury and an attempt to determine the principal location of pain. Hematuria and anuria require careful attention. Blood from the urethra not associated with urination suggests urethral injury distal to the external urinary sphincter. Ecchymoses over the various organs, local tenderness, and masses (from bleeding or urinary extravasation) should be noted. Abdominal paracentesis should be performed if intraperitoneal hemorrhage is suspected. Rectal examination may reveal displacement of the prostate or indications of extravasation such as swelling or bagginess of the tissue about the urethra.

Special X-ray procedures often are useful in diagnosis. A plain film of the abdomen may reveal several important problems: a fractured pelvis, which often is associated with urethral or vesical injury; a fracture of the lower ribs or transverse processes of the lumbar vertebrae, which may indicate injury to the kidney, pelvis, or ureter; or air under the diaphragm, which may denote an injury to a hollow viscus. Perirenal hematoma may be suggested by haziness of the renal outline and obliteration of the margin of the psoas muscle. The excretory urogram may show no function in one kidney or extravasation of the opaque medium in nonhypotensive patients.

A second special procedure which should be followed, if possible, is aseptic catheterization of the urethra and bladder. Bloody urine indicates injury to the urinary tract. The site of the lesions in the urethra or bladder may be located by a urethrogram or cystogram. If no extravasation is seen in the latter X-ray, the bladder should be emptied and another film exposed to eliminate the possibility of overlooking a small extravasation anterior or posterior to the bladder.[4] An unruptured bladder may give a characteristic teardrop appearance if a pelvic hematoma is present.[5]

In the treatment of trauma, prophylactic use of antibiotics is advisable.[4] If, during abdominal exploration, a hematoma or obvious renal damage is found, it is unwise to open the posterior portion of the peritoneum for either further exploration or evacuation of clots unless the hemorrhaging is uncontrollable or the kidney is severely damaged.[6] If bleeding seems to have stopped and the kidney is not completely destroyed, definitive treatment of the kidney can wait until the patient's condition has stabilized and it has been determined whether the kidney will recover spontaneously. In cases of injury to the urethra, when a catheter cannot be passed

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NASSER JAVADPOUR *is a resident at St. Paul–Ramsey Hospital, and* A. A. HAKIM *is clinical director of the Department of Urology at St. Paul–Ramsey Hospital and a research associate in the Department of Physiology at the University of Minnesota.*

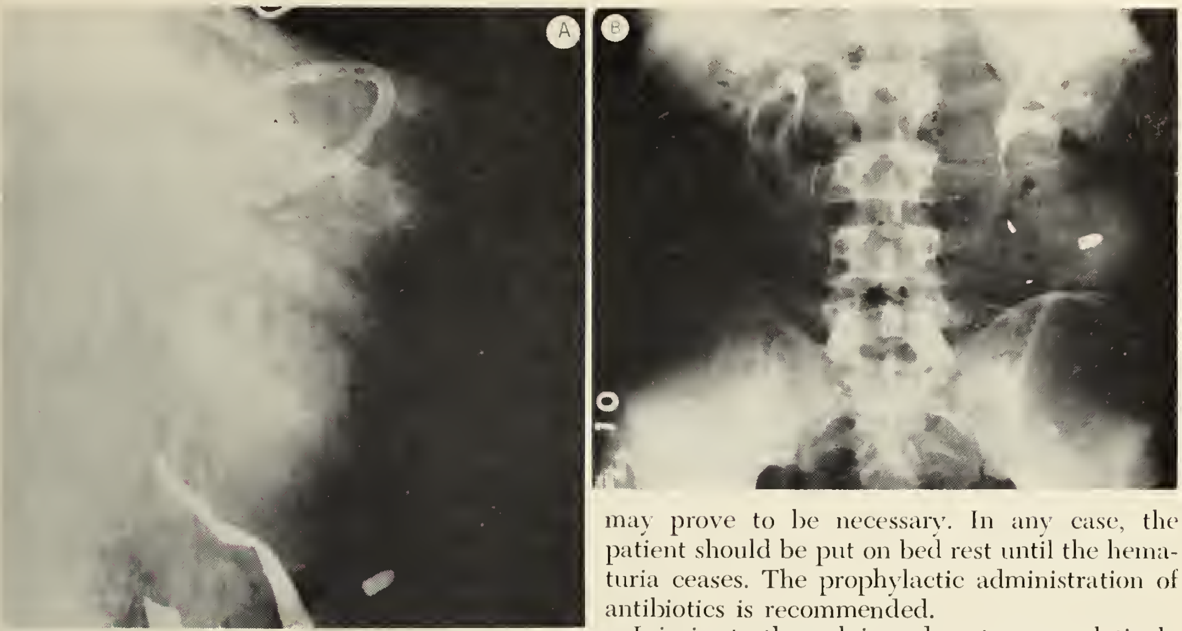

Fig. 1. A gunshot wound of the lower pole of the left kidney. [A] An intravenous pyelogram taken at the operating table shows haziness of the contour of the left kidney, no visualization of the collecting system in the lower pole, and possible extravasation of the contrast medium. [B] An intravenous pyelogram taken ten days after amputating the lower pole of this kidney

to the bladder and general conditions do not permit exploration of the ruptured part, a suprapubic tube can be inserted for drainage. The continuity of the urethra can be established at a later date.

METHODS AND MATERIALS

In order to present a sufficiently detailed discussion of urinary injuries, trauma to the various organs will be considered separately. Renal trauma may be classified as follows: [1] simple bruising and mild laceration of the renal capsule, [2] incomplete fissure of the parenchyma (if this involves the renal pelvis only, hematuria without perinephric hematoma may develop), [3] severe laceration (if the laceration extends through the capsule and the pelvis, extravasation of both blood and urine will occur), and [4] rupture of the renal vascular pedicle (severe bleeding which may prove fatal is a consequence).

In treatment of renal trauma, shock and hemorrhage must be combated first. Conservative treatment is adequate in 80 to 90% of the cases;[7] however, if the vital signs and hemoglobin level cannot be maintained at satisfactory levels by repeated blood transfusions, the injured kidney should be explored before the development of irreversible shock. Drainage of the perirenal space, suture of renal lacerations, or nephrectomy may prove to be necessary. In any case, the patient should be put on bed rest until the hematuria ceases. The prophylactic administration of antibiotics is recommended.

Injuries to the pelvis and ureter are relatively rare. Usual symptoms are an enlarging mass in the flank area and general toxemia. Early diagnosis is the key to successful management of such injuries.[8] A retrograde pyelogram is of special diagnostic value when pelvis or ureter damage is suspected but not confirmed by the usual excretory urogram.

Mild lacerations not involving severance of the ureter may be treated by using a large ureteral catheter as a splint. If there is extravasation, free drainage should be established immediately. In cases involving severance of the ureter, the contused ends may be resected and an oblique end-to-end anastomosis of the healthy segments may be performed. The repaired ureter is then splinted with a small rubber catheter, which may be inserted through a stab wound in the ureter below the laceration and passed up into the renal pelvis. The distal end of the catheter should be brought out through the anterior abdominal wall.

The symptoms of injury to the bladder may be manifested by pain in the suprapubic area, retention of urine, urgency, or hematuria. If the extravasation of urine is intraperitoneal, a rigid abdomen is usually found. Extraperitoneal extravasation may be recognized by a mass in the region of the bladder which can be palpated either suprapubically or rectally. In any case, a properly executed cystogram will lead to the proper diagnosis.

Initial therapy involves the treatment of shock and hemorrhage. Intraperitoneal ruptures are treated by opening the peritoneum, exploring the viscera, and closing the wound intraperi-

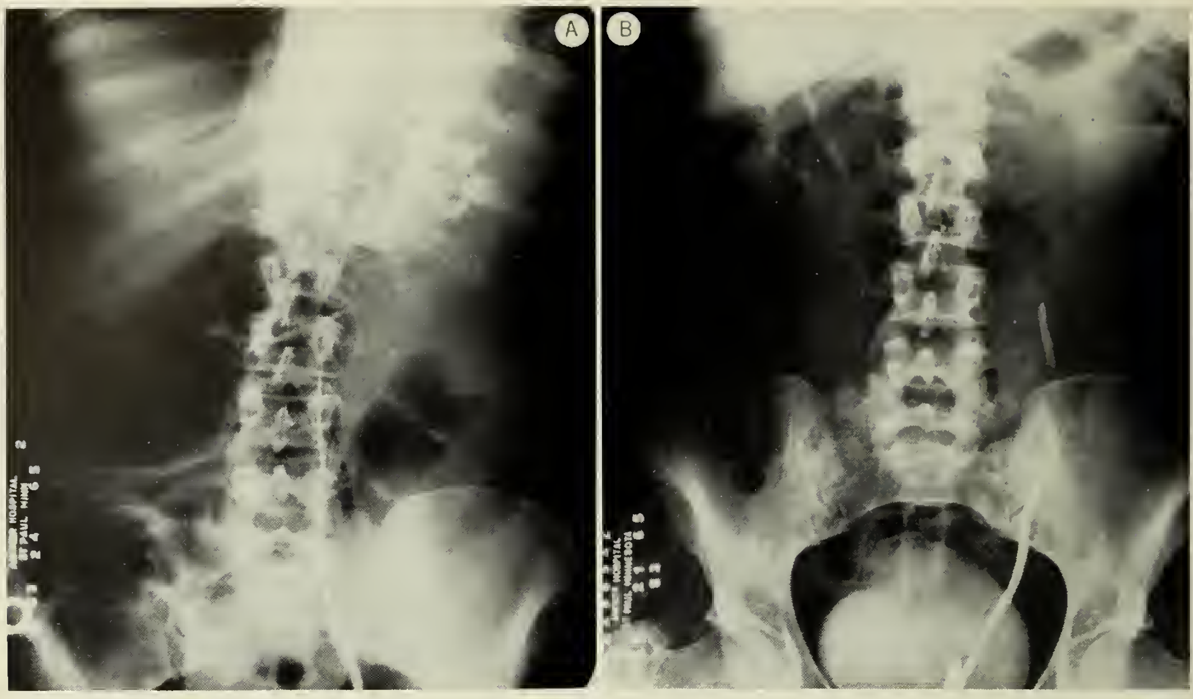

Fig. 2. [A] Extravasation of the contrast medium from the pelvis and possibly from the calyx of the lower pole as seen in a retrograde pyelogram. [B] A bulb retrograde pyelogram which shows the obstruction of the upper one-half of the lumbar ureter secondary to the fibrosis due to the infected hematoma

toneally and intravesically. The peritoneal cavity should be washed thoroughly and closed. Extraperitoneal ruptures are treated by closing the wound intravesically and leaving a drain at the site of the extravasation. A suprapubic tube is left to drain the bladder in both cases.

Injuries to the membranous urethra are caused mainly by crushing or penetration of the urethra by the pelvic bone during motor accidents.[3] This may lead to avulsion of the prostate gland from the membranous urethra. The main complaints are suprapubic and perineal pain accompanied by difficulty in urination. Retention or urethral bleeding also may be present. Rectal examinations will reveal a large, boggy mass of extravasated blood and urine accompanied by upward dislodgment of the prostate gland.[9] Fractured pelvic bones, if any, will be seen in plain X-rays, whereas a urethrogram will display the site of the torn membranous urethra.

For cases of mild lacerations, the treatment requires the passing of an adequately sized catheter to the bladder, where it should remain for two or three weeks. In more serious cases, the prostatomembranous urethra is explored, the blood clot is evacuated, and the 2 ends are defined. An antegrade catheter is introduced from the bladder, and a second one is introduced through the urethra. The 2 catheters meet at the site of the rupture, are tied together, and the urethral catheter is guided to the bladder, where its vesical end is transfixed with stout silk. Both free ends of the silk are brought out through the suprapubic tube. The balloon is inflated and some pressure is applied upon the external end of the catheter to bring the 2 ends of the ruptured urethra in apposition. This procedure is followed if repair by suture cannot be accomplished.

Injury to the bulbous urethra may be caused by falling astride an object. This may lead to contusion or severe laceration. The latter may lead to extravasation of blood and urine into the scrotum, penis, or abdominal wall. The exudate is limited by Colles' fascia.[4] Clinically, a perineal injury may be followed by local pain, some urethral bleeding, and the appearance of a large scrotal mass after an attempt to urinate. A urethrogram may be helpful in giving the diagnosis.

Mild injuries of the type discussed should be left alone. In severe injuries, a catheter should be passed to the bladder if possible. If this cannot be done, surgical exploration and repair of the injured site are mandatory. A Foley catheter should be left indwelling for two to three weeks, and adequate drainage of extensive extravasation should be provided.

Injuries to the penile urethra are most commonly caused by a blow to the penis during erection. Clinically, a periurethral hematoma and bleeding per urethra are encountered. The urethrogram is a useful diagnostic tool.

There is no need for an indwelling catheter if urination is normal. If the hematoma is large, it should be evacuated. Severe bleeding per urethra requires the application of a urethral catheter and tight bandaging of the penis. Extravasation of urine is treated by the simultaneous drainage and splinting effect afforded by the employment of an indwelling catheter, which should remain in place for two weeks.

CASE REPORTS

Case No. 1. A 42-year-old Negro male was admitted to Ancker hospital with a gunshot wound midway between the left costal margin and the umbilicus. There was no apparent exit. Pulse was 100 and blood pressure was 100/60. Examination revealed generalized abdominal and left costovertebral angle tenderness. Percussion revealed shifting dullness, and intraperitoneal paracentesis revealed intraperitoneal hemorrhage. After the patient was transfused with 1,000 ml. of blood, the abdomen was opened and the contents were explored through a left paramedian incision. Five hundred cc. of blood were evacuated. The left lobe of the liver, mesentery of the transverse colon, and jejunum at the Ligament of Treitz had been perforated. In addition, a large left retroperitoneal hematoma was found.

The perforations were repaired adequately, but the retroperitoneal hematoma continued to increase in size. Bleeding through the torn posterior peritoneum did not decrease, in spite of prolonged packing, while the other viscera were repaired. The renal artery and vein were dissected, bulldog clamps were applied to the artery and vein, the hematoma was evacuated, and the area was irrigated. The lower pole of the left kidney was completely destroyed. The necrotic tissue within this area was amputated, and the remainder of the collecting system was closed with 4-0 chromic catgut. The clamps on the vein and artery were removed intermittently to visualize the bleeding vessels, and they were subsequently clamped and stick-tied until adequate hemostasis was achieved.

The parenchyma was approximated using through-and-through mattress sutures of 2-0 chromic catgut. The capsule was closed with a running stitch of 4-0 chromic catgut. The results were good, as verified by the patient's postoperative intravenous pyelogram (Fig. 1).

Case No. 2. A 36-year-old white female was admitted to Ancker Hospital after being involved in a car accident. On admission she had a thready, fast pulse. Her blood pressure was not obtainable. After 2,000 ml. of dextran were given intravenously, her systolic blood pressure rose to 90 mm. Hg, but then started to drop. By that time, blood was available and 2,000 ml. of blood were given in order to maintain her blood pressure around 100 mm. Hg. Her abdomen was distended and, on percussion, showed shifting dullness. Chest X-ray revealed fracture of lower ribs on both sides but no other abdominal abnormalities. The diagnosis of intraperitoneal hemorrhage was made.

Exploratory laparotomy revealed a ruptured spleen and left retroperitoneal hematoma. A splenectomy was done, but the kidney was treated conservatively by the surgeon. We were called eleven days later because of the patient's general septic condition and continuously elevated temperature, which did not respond to antibiotic treatment. An intravenous pyelogram showed extravasation of the contrast medium on the left side.

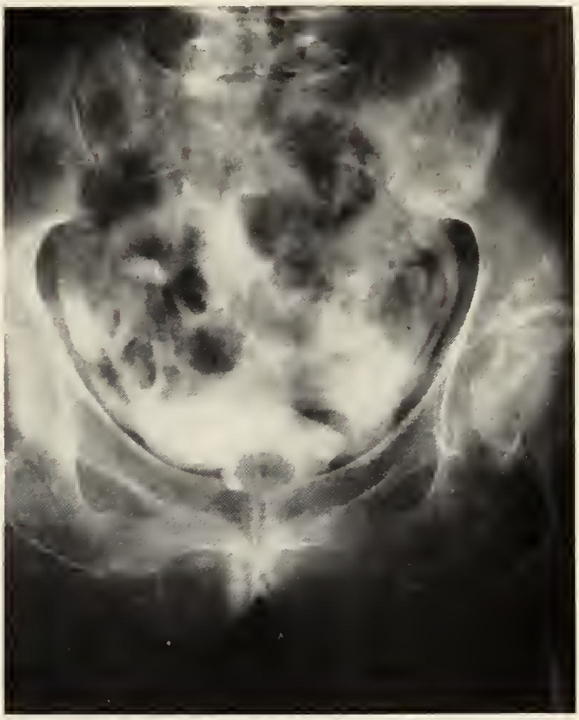

Fig. 3. An intraperitoneal rupture of the bladder. The dye is extravasated outside the bladder and between the intestinal loops.

A retrograde pyelogram showed the site of leakage to be located in the renal pelvis (Fig. 2A). The catheter was left indwelling and the kidney was explored. A large hematoma and urinoma were evacuated, the tear in the pelvis was closed with 4-0 chromic catgut, and multiple Penroses were left to drain the area. Urine continued to drain every time an attempt was made to remove the ureteral catheter. This was due to fibrous tissue which formed around the upper and midureter, secondary to an infected hematoma in this region (Fig. 2B).

Since the patient had a normal right kidney, and due to our failure to eradicate the fistula, a nephrectomy was performed. The patient left the hospital seven days later.

Case No. 3. A 36-year-old white female was admitted to Ancker Hospital after being involved in a car accident. On admission, her pulse was 100 and blood pressure was 112/60. Abdominal examination showed suprapubic tenderness and shifting dullness. Vaginal examination showed no masses, but tenderness was noticed in the area of the bladder. Catheterization revealed bloody urine. A cystogram showed the spread of the contrast media among the intestinal loops (Fig 3). The peritoneum was opened through a midline incision. The bladder and the abdominal contents were explored. A large amount of blood and urine were drained from the peritoneal cavity. The bladder was opened and the edges of the vesical wound were trimmed and closed in 2 layers, 1 intraperitoneally and the other intravesically. A No. 26 Malecot catheter was used to drain the bladder. The peritoneal cavity was irrigated thoroughly and closed. The patient made an uneventful recovery.

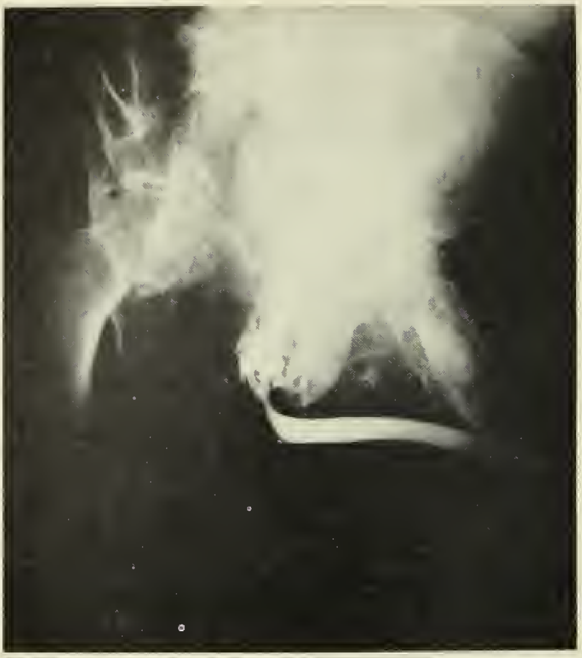

Fig. 4. The avulsion of the membranous urethra after severe fracture of the pelvis

Case No. 4. A 50-year-old white male was admitted to Ancker Hospital after being involved in a car accident. On admission, his pulse was 120 and his blood pressure was 55 systolic. Evidence of multiple fractures of the right leg and pelvis was apparent. After intravenous administration of 2,500 ml. of dextran solution and blood, his blood pressure rose to 120/80. His pulse was 100. The patient regained consciousness. On examination, the abdomen was negative except for suprapubic tenderness and dullness. Rectal examination revealed a large, boggy mass in the area of the prostate. The prostate itself was not palpable. X-rays showed multiple fractures of the pelvis. A catheter was passed with ease to the bladder, and a cystourethrogram was done. It revealed avulsion of the prostate from the membranous urethra (Fig. 4).

The catheter was left indwelling. His blood pressure started to drop and subsequently the patient was transfused with 10 bottles of blood. This did not help to stabilize his blood pressure. Intra-abdominal exploration revealed no injury to the viscera. A very huge hematoma was encountered in the vicinity of the bladder and on the inner surface of the pelvic bones. As much as possible of the hematoma around the bladder was evacuated. The bladder was opened and a Foley catheter was introduced through the urethra. A strong piece of silk was left attached to the tip of the Foley catheter and brought out with the suprapubic tube so that the catheter could be changed if the bag should burst.[1] Slight traction was applied to the catheter to bring the 2 ends of the severed urethra in apposition[4,6,9] and the peritoneum was closed. Severe bleeding around the bladder continued in spite of prolonged packing. The main bleeding was coming from the right hip bone. The right hypogastric artery was ligated at its origin,[10] but the bleeding did not slow down appreciably. Ligation of the left hypogastric artery led to a dryer field.[10] The Retzius space was drained and the abdomen was closed. The patient did fairly well for five days but then died suddenly. Autopsy revealed massive fat embolism.

Case No. 5. A 43-year-old Negro male was admitted to Ancker Hospital after being involved in a car accident. On admission, his pulse was 95 and blood pressure was 100/70. Examination revealed a fractured pelvis, blood per urethra, and a rigid abdomen. Percussion revealed shifting dullness. The surgeon was unable to pass a catheter to the bladder. The diagnosis of intra-abdominal bleeding was made, and, due to his critical condition, the patient was taken immediately to the operating room without having the performance of a cystogram. Explora-

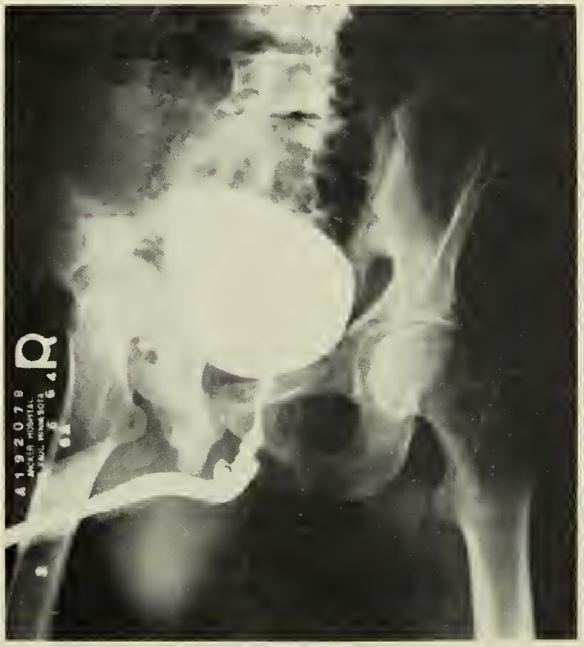

Fig. 5. A cystogram taken a month after splinting showing the irregularity in the bulbomembranous urethra

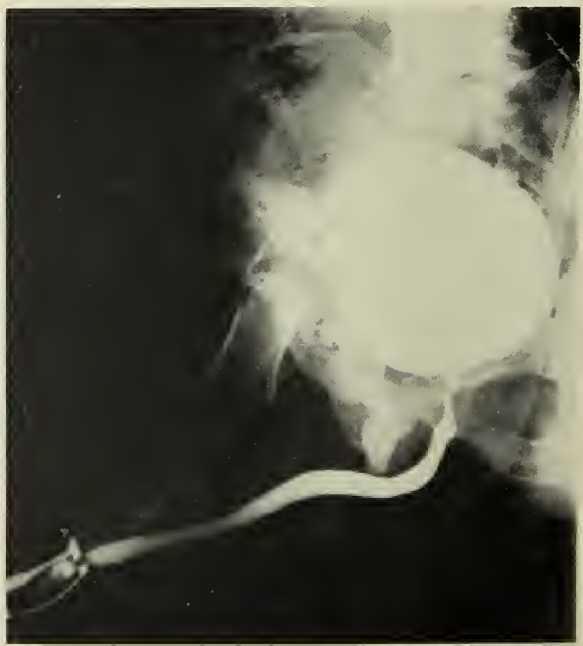

Fig. 6. A cystogram taken three months posttrauma showing complete recovery

tory laparotomy showed a ruptured jejunum which was partially resected. End-to-end anastomosis was performed and a right pelvic hematoma was found which continued to increase in size and bleed severely around the bladder. The right hypogastric artery was ligated near its origin, which stopped the bleeding.[10] The bladder was opened, and a gentle attempt to pass a catheter in an antegrade fashion through the urethra was unsuccessful. Due to the critical general condition of the patient, it was decided to drain the bladder suprapubically and postpone the repair of the urethra until a later date.[9] The Retzius space was drained. Ten days postoperatively, a No. 18 Foley catheter on a stilette was inserted by hugging the anterior wall of the urethra. It slipped with ease into the bladder. The balloon was inflated and the catheter was fastened with a heavy silk stitch to the glans penis. The catheter was left indwelling for a month. During the patient's convalescence, repeated urethral dilations were performed; the results were good (Figs. 5 and 6).

SUMMARY AND COMMENTS

This is a report of sample cases of suspected multiple injuries following severe trauma. They demonstrate how the urologist must always take into consideration the possibility of associated injuries and the general condition of the patient. Our inclination is to treat the patient with trauma to the kidney conservatively, unless circumstances indicate that stronger measures are required. If surgical intervention is indicated, the renal pedicle should be identified and intermittently clamped, which should help in decreasing the blood loss, diagnosing the injury, treating the injury, and achieving superior results. In a patient with associated severe trauma to the bony skeleton, the site of the injury should be immobilized, and the patient should not be moved unless absolutely necessary; otherwise, the primary injury may be brought under control, but the patient may die from fat embolism.

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Blunt and Penetrating Wounds of the Abdomen

HARLAN D. ROOT, M.D.

St. Paul, Minnesota

As a cause of death, accidents lead in the 5- to 25-year-old age groups and are third in importance behind cardiovascular disease and cancer in the ages beyond 25 years.[1] Moreover, the accidental death rate continues rather consistently at 60 to 80 per 100,000 population. In a country of 200 million citizens, the import of these figures is staggering. We shall limit our consideration of this problem to blunt and penetrating abdominal wounds.

Penetrating abdominal trauma, a major problem faced by the military surgeon in wartime, will vary in incidence in the practice of civilian physicians according to the ethnic and economic characteristics of the population served. In those populations where the judicial-executive functions are on a do-it-yourself basis, the ratio of penetrating abdominal injuries to blunt abdominal injuries will be higher than among the group where social, educational, and economic circumstances leave the meting out of justice to the appropriate public officials. In the Ancker Hospital experiences reported by Perry,[2] 60 of 152 or 40% of abdominal injuries were of the penetrating type. In all classes of citizens, however, blunt abdominal trauma resulting largely from automobile accidents and, less frequently, from falls, fists, and athletic injuries exacts its toll.

INITIAL MANAGEMENT

The initial management of a patient who has suffered any type of abdominal injury should be a quick survey of his vital signs, level of consciousness, respiratory status, and other associated injuries, so that priority of treatment can be assigned. A large-bore needle or catheter should be placed in a peripheral vein in the event that the rapid administration of blood should be necessary. For proper initial supportive treatment of massive intraperitoneal or retroperitoneal hemorrhage, prompt, equally massive, and rapid replacement of type O, Rh-negative whole blood must be instituted to maintain at least a minimum perfusion pressure of vital centers until immediate laparotomy offers opportunity for control of the hemorrhage. Type-specific blood can meanwhile be secured. An ischemic arrested heart is difficult to resuscitate no matter how youthful the myocardium. An emergency room which could be called upon to manage grave situations of this magnitude should keep at least 10 units of type O, Rh-negative blood banked within it at all times. Moreover, an operating room should be maintained in the receiving room completely stocked with all necessary supplies, instruments, anesthesia equipment, electrocardiograph machine, and cardiac defibrillator for an emergency laparotomy or thoracotomy. Repeated rehearsals of such a performance should be held so that all personnel, regardless of shift assignment, know their precise jobs and the location of all equipment and supplies. Every assigned physician should know how to give external cardiac massage and how to insert properly and deftly an endotracheal tube and maintain appropriate respiration with either an Ambu unit or a regular anesthesia gas machine. Because a surgery resident should be immediately available to the receiving room, only he and his colleagues should do the actual emergency surgery. His prior specific training will make him most suitable for this responsibility. An alternate plan is used in Louisville, Ky., where all trauma victims are rushed to and evaluated first in the operating room suite where the above maneuvers can be executed. Any such regimen, properly planned, taking into account all exigencies and frequently rehearsed, will decrease the mortality rate in massive injuries. Although many injured patients may die at the accident scene from massive ruptures of the aorta, heart, or liver, other patients with similar type injuries may still be salvageable when

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HARLAN D. ROOT *is from the department of surgery, St. Paul–Ramsey Hospital, St. Paul.*

first seen in the receiving room. With proper planning in receiving room construction and administration, triage should never be necessary.

Further supportive care should be given as indicated for hemopneumothorax, "flail" chest, open fractures, and respiratory obstruction. In cooperation with rescue units, the regimen of retrieving, maintaining, and moving patients on a rigid, padded, radiolucent plywood litter described previously[3] facilitates the management of these patients. Extremity and spine fractures are thus immobilized and the patient is left continuously at rest, preventing the recurrence of further bleeding from fractures, damaged soft tissues, or major vessels. This minimizes further trauma to the injured patient, conserves time and effort in moving him, and can be used to good advantage throughout all diagnostic maneuvers and even in the operating room for the urgent situation posed above.

PENETRATING ABDOMINAL INJURIES

Gunshot and knife wounds are by far the most common type of penetrating abdominal injuries. With the exception of shotgun wounds inflicted at close range, low-velocity bullet wounds and stab wounds do not cause massive tissue damage with its associated high mortality rate as commonly occurs with blunt abdominal injury. Multiple injuries, however, are common in each type of abdominal trauma. The mortality to be expected from penetrating abdominal injuries is about 5%. The major problems of penetrating abdominal trauma are [1] deciding whether or not to explore the abdomen and [2] the choice of corrective procedure for the intra-abdominal damage found.

Dwelling for a moment on the first problem—making the decision whether or not to operate upon the patient with a penetrating injury of or near the abdomen—we find currently in the spectrum of options: [1] at one extreme, explore all patients with possible intra-abdominal damage from the penetrating mechanism[4,5] and [2] at the other extreme, don't explore any patient until obvious clinical signs indicate the necessity of operative intervention, a philosophy expounded by Shaftan[6] and recently by Mason.[7] There are excluded from this diagnostic dilemma patients with the compelling indication for prompt abdominal exploration, that is, profound shock which responds temporarily to blood transfusions, with an expanding abdomen, or a patient with abdominal rebound tenderness and rigidity. Blood found in the rectum, bladder, or stomach after a penetrating abdominal injury is usually indicative of damage to the viscus.

At a midpoint on this scale of options is the utilization of diagnostic maneuvers which may help decrease the number of unnecessary abdominal explorations.

To this end, Cornell[8] has reported an interesting diagnostic maneuver for the evaluation of stab wounds to detect penetration into the abdominal cavity. He does not recommend its application for gunshot wounds. A No. 14 F catheter placed into the wound tract is secured there by a 2-0 silk purse string in the skin around the entry site. Thereupon, 60 to 80 cc. of 50% diatrizoate (Hypaque®) containing 1 cc. of methylene blue is injected into the catheter, following which the patient is rolled from side to side. Abdominal X-rays are then taken in anteroposterior and lateral planes. If the peritoneum has not been breached, the dye is seen to layer in the extraperitoneal planes outside the abdominal cavity and causes no complication thereby. Of 24 patients studied, dye entered the peritoneal cavity in each of 9 patients through the stab wound and was confirmed at laparotomy. Fourteen patients showed no evidence of intraperitoneal dye. There were no false-negative results. Only 6 of this latter group of patients underwent abdominal exploration. In the face of these statistics, he still advocates abdominal exploration in all patients with penetrating abdominal injuries until further experience warrants acceptance of this technique.

Another experimental diagnostic technique used routinely in blunt abdominal trauma is that of diagnostic peritoneal lavage described previously.[9] The abdomen is lavaged with isotonic saline or inpersol solution via a special catheter placed in the abdominal cavity through a trocar. The recovery of significant amounts of blood, enteric debris, bacteria, or leukocytes from the returning perfusate may be indicative of visceral damage, thus improving the precision of diagnosis. Whether or not this technique will be of reliable help in choosing for exploration patients who have suffered penetrating abdominal injuries cannot yet be told. Further work in this study is under way. Whatever the option exercised, there should be no greater mortality or morbidity than realized in the group explored immediately and found to have visceral damage. Hopefully, morbidity created by negative abdominal explorations under option 1 or 2 could be avoided.

In summary, we believe that for the present time, until reliable diagnostic techniques are available, all patients who have suffered penetrating injuries from any object which could have entered the abdominal cavity should undergo early abdominal exploration.

At this junction, it seems fitting to urge that at the time of operation very careful examination of the entire small bowel, duodenum, and colon millimeter by millimeter be done lest small rents be overlooked with disastrous consequences. Retroperitoneal hematomata found under these circumstances should be explored for possible concomitant damage of the inferior vena cava, aorta, or some other large vessel.

COLON INJURIES

As to the treatment of specific injuries from penetrating wounds of the abdomen, colon injuries are worthy of comment because of the controversy regarding them. Whereas exteriorization of the damaged area of colon or creation of a proximal diverting colostomy is still standard procedure for wartime military surgeons, colon injuries in the civilian populace are usually treated by primary closures of the colon wound unless massive or prolonged peritoneal fecal contamination, or both, with multiple areas of colon damage has occurred. The mortality from this technique is actually lower than with routine exteriorization of colon or colostomy creation according to Vannix.[10] In his study of 46 patients with primary venting procedures, 24% died, whereas of 76 patients with primary closure of the injured colon only 6% died. Perry[2] recorded 10 patients with penetrating colon injuries, 9 of which were treated by primary closure or resection and anastomosis with 100% survival. Because of the high incidence of wound infection under these circumstances of contamination, the fascia should be closed with figure eight, No. 26, stainless steel wires, and the skin should be closed secondarily several days later by tying the wire skin sutures placed during the initial operation to prevent wound infection. The morbidity and risk of the situation are thereby greatly reduced.

By comparison with blunt abdominal trauma the mortality from penetrating wounds of the abdomen is low but could easily be halved as judged from our own experiences[2] and that of others.

BLUNT ABDOMINAL INJURY

Of all forms of trauma, blunt abdominal trauma accounts for the greatest number of deaths, although percentagewise, severe head injuries are the most lethal. The stated mortality of 45.7% from blunt abdominal trauma at the Ancker Hospital[2] is representative of many series and thus is worthy of further consideration. The high mortality is due to several factors among which are undiagnosed visceral injuries, massive multiple organ injuries, inadequate blood replacement, delay in initiating appropriate supportive measures such as tracheostomy, and associated lethal head or chest injuries. Pertinent to several of these factors was the introductory discussion of general management of abdominal injuries.

The less urgent but more frequently encountered type of patient has suffered blunt abdominal trauma often coupled with head or chest injuries and is dazed, confused, or perhaps comatose. The diagnostic dilemma once again arises. Does the patient have significant intra-abdominal injury? A dulled sensorium or coma and fractured ribs render abdominal signs difficult to interpret. The presence of multiple, potentially lethal, injuries often including a "flail" or unstable chest wall and head injuries precludes the routine performance of a laparotomy on all of these patients because of their precarious condition. Perry[2] has shown that the admission peripheral hemoglobin concentration and leukocyte count are of no help in making the diagnosis of visceral injury. Abdominal paracentesis with a No. 18 needle in 4 quadrants usually produces 10 to 50% false-negatives. Undiagnosed abdominal visceral injury accounted for 7 of 42 deaths at Ancker Hospital.[2] To obviate this defect in our patient management we employ routinely the new technique of diagnostic peritoneal lavage,[9] described above with penetrating abdominal injury. Lavaging the abdomen with saline through a catheter will disclose even very small amounts of intraperitoneal blood loosed at any point in the abdomen which then serves as an indication for laparotomy. The returning perfusate, when not bloody, should be centrifuged and the sediment strained for enteric debris, bacteria, and leukocytes. We have found an early, profound, intraperitoneal leukocytosis in the presence of a perforated ileum and in retroperitoneal rupture of the duodenum. Of over 100 consecutive patients with possible intra-abdominal injury, diagnostic peritoneal lavage has correctly indicated visceral damage without false-negative results. The peritoneal leukocytosis was not correctly interpreted in a child with a ruptured ileum, fractured pelvis, and lower anterior abdominal wall hematoma. No other intraperitoneal visceral damage has been missed since this technique has been utilized, which, for our institution at least, has been a significant improvement in our management of these patients. Certainly, early detection of these visceral injuries can reduce the high mortality rate of blunt abdominal trauma. We have been able, through early detection, to remove ruptured spleens and to repair liver lacerations and bowel damage before hemorrhagic shock has occurred and before peritoneal contamination has resulted in a generalized peritonitis.

BLUNT LIVER TRAUMA

Because of the massive amount of tissue injury which these patients usually have suffered from blunt trauma, management of their specific injuries is more complex than in the instance of a knife wound. Liver disruptions from blunt trauma are often massive with large areas of fissured liver found. Resection of nonviable liver tissue remains the procedure of choice whether a subsegment or lobe is involved. Experience has shown meticulous care in obtaining vascular and biliary stasis of the liver's cut edge with fine nonabsorbable sutures to be preferable to mass ligature or packing. Decompression of the biliary tree by common bile duct drainage or, in the event of a very small common duct, by cholecystostomy should be employed routinely for all liver lacerations requiring more than one suture for reapproximation. Temporary drainage of the subhepatic space by sump or Penrose drains is commonly employed. A phenomenon yet to be satisfactorily explained in the severely injured patient who has, among other things, a "flail" chest is the occurrence of fatal liver necrosis about five to seven days after injury, even though no obvious external trauma of the liver has occurred.

DUODENAL RUPTURE

One of the uncommon but more difficult diagnostic and therapeutic problems is the patient who may have suffered immediate or delayed retroperitoneal rupture of the duodenum. Intramural hematomas of the duodenum may progress to necrosis of the duodenal wall. This catastrophe may accompany injuries to other viscera such as the liver, pancreas, or small bowel. Oftentimes, it is an isolated injury from some seemingly "minor" but localized blunt trauma as from a rake handle, bedpost, or steering wheel. Moreover, transection of the common bile duct at its point of crossing the duodenum has been reported by Dorton[11] and Kalderon.[12]

Delayed diagnosis of duodenal rupture may be made by clinical signs of peritoneal irritation or flank tenderness as the enzyme-rich duodenal juices dissect into retroperitoneal tissues. Diagnosis by X-ray is possible if air dissects around and outlines the right kidney or the psoas muscle as described by Rigler[13] or if a localized pocket of air with a fluid level develops near the third part of the duodenum as in a recent case of ours. The crepitation of presacral air may be elicited on rectal examination. Extraperitoneal air encountered upon opening the abdomen is indicative of rupture of a retroperitoneal viscus.

A more direct and prompt diagnostic approach should be used in any patient who might have duodenal damage. Through the nasogastric tube which we routinely employ for gastric decompression in all injured patients, 60 cc. of diatrizoate methylglucamine (Gastrografin®) can be injected and a portable flat plate of the abdomen taken five minutes later. Obstruction or rupture of the duodenum may thus be shown early.

At the time of laparotomy in any injured patient, mobilization and complete examination of the duodenum are mandatory, especially if any retroperitoneal hematoma is noted. A Kocher maneuver and incision of the peritoneum at the ligament of Treitz can provide such exposure. Almost 20% of duodenal injuries have been overlooked in the experience of Cocke,[14] attended by a 77% mortality.

Closure of a ruptured duodenum by a simple 2-layer technique or by drainage of the duodenum through a Roux-Y limb accompanied by extensive external drainage of the region has, together with early diagnosis, lowered the expectant mortality to about 20%.

BLUNT TRAUMA OF THE PANCREAS

The mortality from injuries to the pancreas is surprisingly low, varying from 0 to 20%,[15,16] except in those patients with complete pancreatic transection when the mortality may reach 66%. In most cases, the pancreas is bruised, perhaps severely, but viable. Serum amylase level determinations are very helpful in diagnosis, but possible confusion with duodenal or jejunal disruption is to be kept in mind. A persistent elevation of or rising serum amylase level later than five days postinjury is usually associated with a developing pancreatic fistula or pseudocyst or pancreatic abscess. An elevated serum amylase level per se is not an indication for laparotomy but, rather, the clinical circumstances of the patient must be the determining factor. At laparotomy debridement of nonviable tissue is in order combined with sump and Penrose drainage of the pancreatic area for at least two weeks. Complications such as temporary pancreatic fistula, peripancreatic abscess, pseudocyst formation, or subphrenic infections are to be anticipated. The fistulas usually close within two to four weeks. Anticholinergic drug therapy is recommended.

For complete transection of the pancreas, anastomosis of the transected duct ends to a jejunal Roux-Y limb is usually successful[15] if the distal fragment of pancreas is large and viable.

Needless sacrifice of large segments of injured, though viable, pancreas is to be avoided because of the subsequent potential exocrine and endocrine pancreatic insufficiencies.

SUMMARY AND CONCLUSIONS

Although we have considered a number of aspects of both penetrating and blunt abdominal trauma, these injuries are usually only part of the total problems of the injured patient. Oversimplification would be an injustice. Total management of these patients should be directed by a team captain whose breadth of knowledge and experience helps him evaluate the relative risks of the multiple injuries often incurred. It would seem that a general surgeon in most instances could most effectively fill this role, although in some institutions a neurosurgeon or orthopedic surgeon with a background of general surgery might be well suited to this task. Local trauma committee functions can help in such decisions.

Emphasis has been placed on precise and early diagnosis of intra-abdominal injuries. Sir Heneage Ogilvie commented anent this:[17] "Humiliating experiences have taught surgeons that in abdominal emergencies the difference between the best and the worst surgery is infinitely less than that between early and late surgery and that the greatest sacrifice of all is the sacrifice of time." A well-conceived, coordinated, and smooth-functioning plan of management of the injured patient will improve his chances of survival.

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Vascular Trauma

MAX E. HARRIS, M.D.
St. Paul, Minnesota

TREATMENT OF PATIENTS sustaining trauma requires knowledge of the repair of vascular injuries. The concept of controlling hemorrhage is well known, while the established technique of restoration of continuity to blood flow in injured vessels is relatively recent.[1] The survival and normal function of those who have had major vascular trauma is steadily improving due mainly to prompt recognition and surgical repair. The utilization of blood transfusions, modern anesthesia, antibiotics, synthetic graft material, and extracorporeal circulation has made this possible. The majority of patients with vascular trauma have associated injuries requiring evaluation during the institution of therapy. The establishment of an adequate airway, tamponade of obvious external hemorrhage, the prompt closure of open-chest wounds, the insertion of large bore intravenous catheters, and the insertion of intercostal catheters for hemopneumothorax are an integral part of treatment. The utilization of volume expanders or 0-negative unmatched blood, or both, while awaiting that properly cross matched, may be necessary to counteract hypovolemic shock.

The diagnosis of injury to major peripheral vessel is accomplished by physical examination and in some instances by arteriography. The findings of a hematoma with ischemic manifestations distal to the swelling suggest major injury. A diminished or absent pulse associated with blanching, cyanosis, hypesthesia, and, perhaps, diminished motor function strongly suggest arterial damage. Arteriography is of value in equivocal cases or when associated arteriosclerotic occlusive disease is suspected.

These basic precepts must be accomplished with dispatch and during the initial general evaluation. If shock is profound and external signs of bleeding do not explain the degree of shock, attention is directed to the thorax and abdomen for evidence of concealed hemorrhage. Neurological examination is essential to rule out brain injury; however, the cause of shock is seldom intracranial damage.[2] The evaluation and initial treatment is accomplished in the emergency unit en route to the operating room.

WOUNDS AT BASE OF NECK

Major vascular injury is likely in penetrating wounds of the neck and supraclavicular area, and because of this fact, most wounds here should be explored.[3] During the Korean War, if a hematoma in this area was self-contained and hemorrhage controlled, the recommended treatment was observation, particularly if an A-V fistula was present.[4] The wounds were superficially debrided, being careful not to dislodge the clot, and definitive repair was done later. It was thought that even if the patient bled again his chances for survival were better than if immediate definitive surgery was done. Current surgical treatment is immediate exploration and primary repair of the injured structures.[5] Because of the proximity of the chest, associated intrathoracic injuries should be suspected and appropriate measures instituted. A tracheotomy may be advisable because of compression to the trachea. Proximal and distal control of the injured vessel is the primary consideration after the hemorrhage is controlled with pressure. A thoracotomy, utilizing an anterior third intercostal space incision, may be required especially if the subclavian artery is injured proximally. Exposure of the subclavian artery by the subperiosteal resection of the proximal half of the clavicle has been reported.[6,7] This is particularly suited to injuries of this vessel associated with fractures of the clavicle. The technique of the repair after controlling the vessel may be lateral arteriorrhaphy with or without patch angioplasty, utilizing autogenous vein or synthetic material (Fig. 1). If an adequate lumen is not possible after debridement of the edges, then end-to-end anastomosis or graft replacement with autogenous vein or synthetic material is recommended. During repair of carotid artery injuries, internal shunting to reduce cerebral complications is recommended where

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MAX E. HARRIS *is from the Department of Surgery, St. Paul–Ramsey Hospital, St. Paul.*

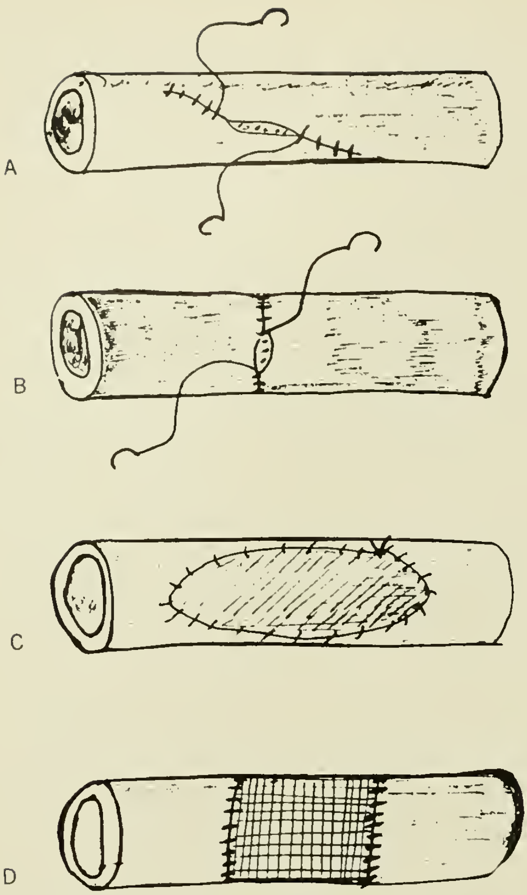

Fig. 1. Four methods of vascular repair. [A] Lateral arteriorrhaphy, [B] end-to-end anastomosis, [C] patch angioplasty utilizing autogenous vein or synthetic material, and [D] graft replacement utilizing autogenous vein or synthetic material.

cross clamping is necessary[5-8] (Fig. 2). Local intra-arterial saline solution of heparin is utilized during cross clamping. The accompanying veins should be repaired if feasible, and if not, they are ligated. Ligation of the subclavian artery resulted in amputation in 28% of the cases and death or permanent brain damage in 30% of the carotid artery ligations in DeBakey and Simeone's[9] experience, indicating the desirability of restoration of continuity. The mortality rate of injured carotid arteries according to Beall and associates[5] was 20%, and of a group of injuries to vascular structures at the base of the neck reported by Patman and associates,[3] it was 20%.

ABDOMINAL WOUNDS

Because of the centrally protected location of major vascular structures of the abdomen, most cases have associated injuries which require therapy.[10] Repair or resection of injured gastrointestinal structures and allied organs is frequently necessary. Smaller vessels with adequate collateral channels may be ligated, but the aorta and most of its major branches require repair. Inferior vena cava injuries above the renal veins must be repaired, and repair is preferable to ligation when the injury is below them. Patients with a history of penetrating injury and many patients with blunt abdominal trauma presenting in shock, with abdominal tenderness and absent bowel tones, warrant exploration. After withdrawal of blood for typing and cross matching, 30 cc. of 50% diatrizoate (Hypaque®) may be injected for intravenous pyelography. The intravenous cannulas for blood and fluids should be placed in the upper extremity in suspected intra-abdominal injuries because of the possibility of inferior vena cava injuries, in addition to the usual reasons for not placing them in the legs. X-ray of the abdomen either en route or in surgery is advised, except in dire circumstances, to determine the status and number of kidneys. The utilization of peritoneal lavage[11] in blunt trauma of the abdomen has been very valuable and more accurate than the conventional four-quadrant needle tap when utilized at the St. Paul–Ramsey Hospital.

Control of the hemorrhage by compression while suctioning free blood and clots is necessary. Proximal and distal control of injured major vascular structures is essential, following which vascular clamps are applied and repair accomplished by the appropriate method (Fig. 1). Repair of aortic lesions can often be attained by debridement of the edges and lateral aortorrhaphy. Patch angioplasty or synthetic grafts may be necessary if more extensive damage is present. Major branches such as the celiac axis, superior mesenteric, renal or inferior mesenteric arteries may be repaired by primary suture if adequate lumen can be attained and, if not, by debridement of the damaged section and end-to-end anastomosis. If the length of damaged vessel is extensive, an autogenous vein may be utilized. Exploration of retroperitoneal hematomas is advised to ascertain their cause, and repair of injured major vascular structures is advised.[3-10]

In one series of penetrating wounds of the thoracic and abdominal aorta, the survival rate with operation was 30%.[12] A similar study in injuries of the superior and inferior vena cava revealed a survival rate of 49%.[10]

Case 1, A53263. A 26-year-old white male was admitted to the Ancker Hospital Dec. 1, 1961, after being shot in the abdomen at close range by a robber. His blood pressure was 130/60 and his pulse was 120. He was alert and complaining of abdominal pain. An entrance wound of the bullet was present in the epigastrium and no exit site was present. There was tenderness and rigidity over the entire abdomen and bowel tones were absent. The patient was given volume expanders and blood and taken to the operating room and exploration of the abdomen performed. A large amount of blood was present in the peritoneal cavity and three perforations of the small bowel, relatively close together, were found and resected, reestablishing continuity by end-to-end anastomosis. Tracing the path of the bullet revealed a 1- by 1.5-cm. laceration in the inferior vena cava below the renal veins. Utilizing pressure above and below the rent, the wall of the vein was sutured with running 5-0 silk suture. The hemorrhage was well controlled and the abdomen was closed. Postoperatively, the patient developed a paralytic ileus and a wound infection, both of which responded to conservative treatment, and he was discharged Dec. 21, 1961.

Comment. Multiple injuries are frequently present within the abdomen sustaining trauma, and a thorough exploration must be accomplished in addition to repairing the obvious damage. The expeditious manner in which this case was managed accounts for the relatively smooth postoperative course and the survival of the patient.

EXTREMITIES

The accessibility of large vessels of the extremities should allow prevention of exsanguinating hemorrhage. The restoration of adequate blood flow for normal function is the ultimate goal. Associated bone and nerve injuries due to the anatomical proximity are frequent. The sudden cessation of arterial flow by ligation of major vessels of the extremity in World War II reported by DeBakey and Simeone[9] indicates a 42.8% amputation rate. When these wounds had an associated fracture, the amputation rate was 60.4%. The more distal the ligation, the lower the amputation rate. The upper extremity due to its rich collateral circulation potential resulted in less amputations than the lower. Ligation of the popliteal and femoral arteries resulted in amputation in 75 and 72.7%, respectively, with associated fractures, and 67.4 and 51.5%, respectively, without fractures. In contrast, the amputation rate in the axillary and brachial artery was 42.8 and 30%, respectively, with fractures and 25 and 11.1%, respectively, without fractures. If the vessel is interrupted below the profundus branch of either the femoral or brachial artery, the amputation rate is lower. In the reported studies of the Korean War injuries, when vascular repair rather than ligation was the treatment, the amputation rate was 11%.[4-13]

Exploration for definitive therapy should be accomplished as quickly as possible to prevent death from hemorrhage (Case 2) and other complications such as false aneurysms, A-V fistulas, delayed hemorrhage, and distal thrombosis. Repair should, however, be attempted in most all cases regardless of time elapse, unless frank gangrene and sepsis are present.[3-13] Hughes[4] states the smaller branches in the leg and forearm often can be safely ligated if it be only one of the usual paired arteries. Jahnke and Seeley,[13] however, report a 16.6 and 33.3% amputation rate with ligation of the anterior tibial and posterior tibial arteries, respectively, indicating the desirability of repair if at all possible. The repair is accomplished by the appropriate method (Fig. 1), and in smaller vessels, interrupted sutures may be superior to running ones. The vessel wall is usually damaged further proximal and distal than is apparent, and it has been recommended that a centimeter of vessel on either side of the injury be sacrificed to minimize failure secondary to narrowing and thrombosis.[14] Freeing of the main channel from surrounding attachments for several centimeters often allows for primary end-to-end anastomosis.

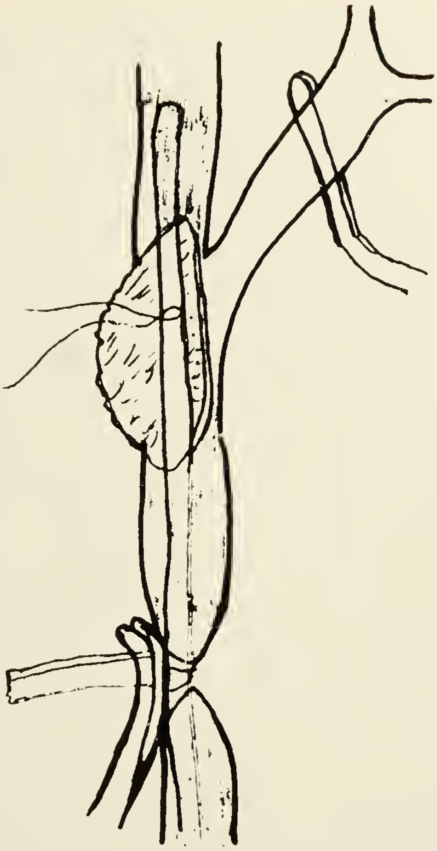

Fig. 2. A method of internal shunting of the internal carotid artery when cross clamping is required. Note the external carotid artery is clamped. Flexible polyethylene tubing as used for a nasogastric tube is suitable.

The value of arteriography depends on the character of the injury.[14,15] Closed wounds asso-

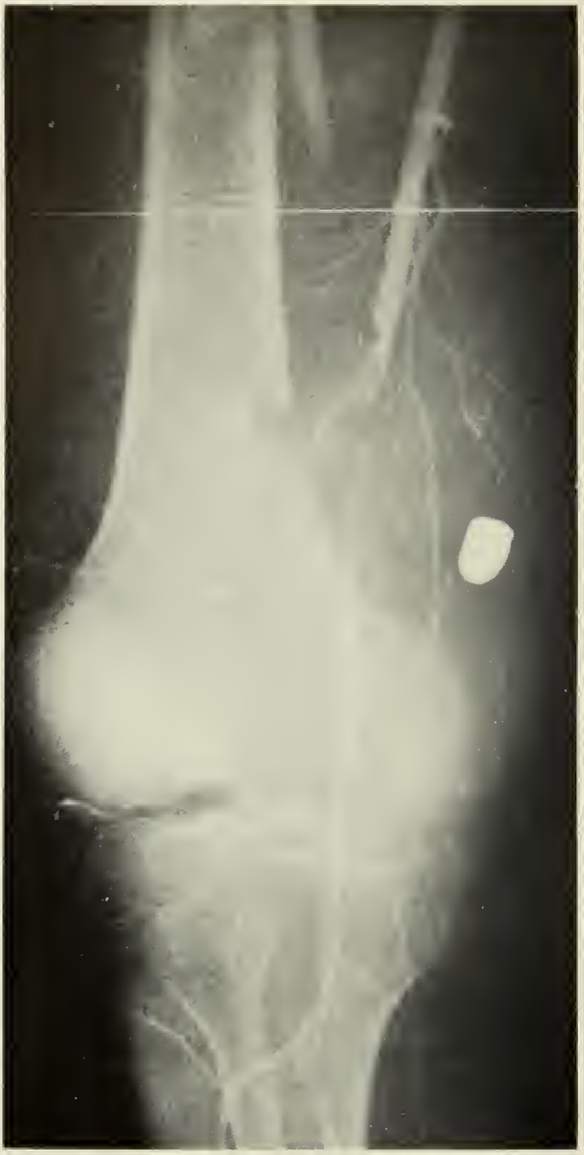

Fig. 3. Arteriogram of Case 3 showing loss of continuity of the superficial femoral artery and retrograde filling of the distal segment. Note the fracture at the top of the photograph and the defect in the cortex on the medial aspect of the femur just above the condyle.

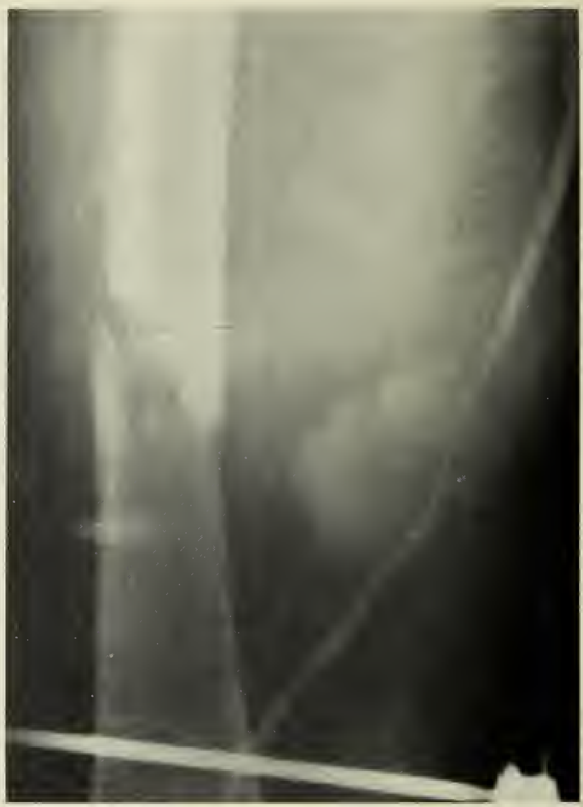

Fig. 4. Arteriogram of Case 4 demonstrating a false aneurysm of the superficial femoral artery and extensive hematoma of the thigh. A fracture of midfemur is evident.

ciated with dislocation or fractures especially around the knee and elbow lend themselves to arteriography, since ordinarily hemorrhage is contained and the emergency is not quite as urgent. The site and approximate extent of the injury as well as the existing collateral circulation can be evaluated (Case 3). In late cases, where false aneurysm (Case 4) or A-V fistulas are suspected, it supplies added information.

Older patients who may have existing arteriosclerotic disease may require more than the usual physical findings to evaluate the preoperative as well as the postoperative status.[14] It has been emphasized repeatedly that the diagnosis of arterial spasm be made with caution.[14-16] Exploration and demonstration of restoration of flow without injury after application of 2.5% papaverine packs or injection of saline under pressure, or both, have been suggested.[13-15] Probably, most of these lesions are contusions with subintimal dissection and obliteration of the lumen, and resection with end-to-end anastomosis would be advisable. When the area is extensive, a bypass graft has been used.[8]

Veins should be repaired when possible, and if not, they may be ligated to control hemorrhage. Loss of the limb is occasionally due to venous stasis after ligation.[4] Fasciotomy is advisable in all compartments of the involved limb at the time of repair if marked swelling is anticipated.

Case 2, A265718. A 25-year-old white male was admitted to Ancker Hospital Sept. 17, 1962, because of an injury of his right arm after being caught in a conveyor belt. His blood pressure was 180/90 and his pulse was 110. There was a laceration through the right axilla, and soft tissue of the shoulder and upper arm was exposed. There was an obvious compound comminuted fracture of the midshaft of the humerus. The right axillary pulse was palpable, but no pulses were present in the antecubital space. The forearm and hand were moderately cyanotic and cool. At surgery, the axillary artery was found to be completely divided. The major veins and nerves were intact. After irrigation, vascular clamps were placed on the artery proximally and distally. Intramedullary fixation of the humerus was accomplished after a small portion of bone had been removed to allow more adequate vessel length. An end-to-end anastomosis of the axillary artery was done, utilizing running over and over suture of 5-0 silk. Intra-arterial heparin solution was utilized locally during the repair, and a radial pulse was present postoperatively and has remained.

Comment. This case illustrates the frequent association of vascular and orthopedic injuries and a method of obtaining fixation and added length of vessel for primary repair. Although the limb may have been salvaged with ligation alone, the functional result of the limb is likely to be better with restoration of arterial flow through the main artery.

Case 3, A117458. A 24-year-old white male was admitted to Ancker Hospital Aug. 4, 1963, having sustained a pistol shot in the left leg just above the knee at 6 A.M. on the day of admission. The patient was cool and clammy, and profuse diaphoresis was present. The blood pressure was 110/50 and pulse 96. There was swelling, deformity, and crepitation in the area of the middle third of the left femur. The leg was cool and pulseless from the groin distally. Intravenous catheters were placed, following which dextrose and blood were administered and the blood pressure and pulse stabilized. Left femoral arteriogram was done, revealing disruption of continuity of the left superficial femoral artery (Fig. 3).

At surgery, an incision was made on the medial aspect of the leg extending above and below the knee. Proximal and distal control of the superficial femoral artery was obtained, following which the femur was stabilized with Rush's pins. The vessel was then debrided approximately 1 cm. on either side of the disrupted site and an end-to-end anastomosis was accomplished with running over and over 5-0 silk. Before closure of the last sutures, retrograde flushing through the posterior tibial arteriotomy was accomplished. Following the repair of the posterior tibial arteriotomy and the release of the clamps, good pedal pulsations were present. Postoperatively, the patient developed stiffness of the knee and peroneal palsy requiring extensive physical therapy and orthopedic manipulations. He was treated for pulmonary embolism with anticoagulants. The pulses of good quality have remained.

Comment. The value of arteriography in ascertaining the exact site of vascular injury and the state of the collateral circulation as well as the associated bone injury is illustrated.

Case 4, A257799. A 40-year-old Negro male was admitted to Ancker Hospital July 9, 1965, at 7:00 P.M. He had a strong odor of alcohol and had been hit by a car. He complained of pain in his right leg. His blood pressure was 60/?, and the radial pulse was 100. There was obvious deformity of the right femur and distal one-third of the right leg. There was a 1-cm. laceration of the lateral calf in the area of the fracture. O-negative blood was administered, and the blood pressure dropped to 80 systolic and his pulse rose to 114.

A peritoneal lavage revealed bloody fluid, and the patient was taken to surgery, where an exploratory laparotomy revealed a ruptured spleen and bleeding from smaller mesenteric vessels. A splenectomy and small bowel resection were done. Postoperatively, the patient had traction applied to the right femoral fracture, and because of inability to obtain proper alignment, Steinmann's pins were inserted into the femur to facilitate alignment.

Two days postoperatively, on July 23, a large hematoma associated with pain was noted in the right thigh. Good pulsations in the dorsalis pedis and posterior tibial artery, together with a warm foot, were noted. The bleeding was thought to be secondary to the manipulation, and conservative therapy was advised. The patient spiked a temperature to 102° F. for several days, and it was felt the hematoma was infected. The patient was given whole blood, but his hemoglobin continued to drop, being recorded on several occasions between 6 and 9 gm. An arteriogram (Fig. 4) was done, and a false aneurysm was noted. On Sept. 7, ligation of the superficial femoral artery was done to control hemorrhage. On Sept. 8, the leg was pale and appeared very ischemic, and in spite of the known risk of grafting due to the probable infected area, a femoral popliteal bypass graft, utilizing a knitted Dacron, 8-mm. tube graft, was done. Peripheral pulses were excellent postoperatively. A febrile course ensued, and hemorrhage from the popliteal wound required an A-K amputation. The patient subsequently required removal of the graft left in place at the time of amputation and revision of his amputation site.

Comment. The exact time of injury to the femoral artery is difficult to determine. However, there were no symptoms referable to the vascular structures until after the manipulation of the fracture. The arteriogram was a valuable diagnostic aid in this instance to delineate the exact nature of the injury. This case exemplifies a futile attempt to save a limb against almost unsurmountable circumstances.

Case 5, A145048. A 44-year-old alcoholic Indian male was admitted to Ancker Hospital at 10:30 P.M. on July 10, 1959, after being found by police and apparently having been hit by an automobile. He was semistuporous, and his blood pressure was 84/50 and his radial pulse 110. A small amount of epistaxis was present and a small laceration was present on the head. A compound, comminuted fracture of the left tibia and fibula was present. There was a large hematoma present in the left groin. The patient was given dextrose and 1,000 cc. of whole blood and expired three hours after admission.

At autopsy, the pertinent findings were marked edema of the left groin and leg, a compound comminuted fracture of the left tibia and fibula, slight pulmonary edema, and, the primary cause of death, a complete severance of the left common femoral artery with massive hemorrhage into the left groin and soft tissues of the retroperitoneal space, estimated at 5,000 cc. of blood.

Comment. This case exemplifies the necessity of immediate preparation for and the accomplishing of definitive repair in vascular injuries of major vessels.

(Continued on page 311)

Perforations of the Colon and Rectum

WILLIAM C. BERNSTEIN, M.D.
St. Paul

It has long been recognized that the early scriptures reveal much information related to the fields of medicine and surgery. In the field of colon surgery, we learned in the book of Judges that Ehud, a left-handed man, stabbed Eglon, the King of Moab—"and his dirt ran out and he died."

Hippocrates,[1] the celebrated physician of antiquity, saw many colon wounds and regarded them as "deadly." Celsus said that the cure of such wounds should be left to nature. In medieval times, murder was often accomplished by introducing a sword through the anus and producing a perforating wound of the colon. This technique was used particularly in the murder of prominent personages. It was possible for the assassination to be concealed, for death would ensue from peritonitis in a few days without any external evidence of injury. Opening into the colon of a sheep or a horse suffering from obstruction is a veterinary operation which has been practiced for many centuries.

This cursory review reveals that perforations of the colon have always been regarded as exceedingly serious and that in former eras a fatal outcome was to be expected. Although the prognosis of untreated perforations of the colon is as poor today as in days past, treatment of these injuries by current surgical and medical procedures after early diagnosis insures a high percentage of successful recoveries.

Perforating wounds of the rectum and colon occur far more frequently during military combat than during times of peace. In World War I, these wounds were accompanied by a tragically high mortality of about 50%. However, with the inauguration of better surgical treatment, together with the development of chemotherapy and antibiotics, mortality during World War II dropped to about 10%. Anesthesiologists, with their ever increasing skills and improved anesthetic agents, have contributed greatly to the improved statistics in this field of surgery. At the present time, excellent rates of recovery can be anticipated in many cases of colon perforation.

This decisive shift from the dismal prognosis of a few years ago to the relatively optimistic note of today can be illustrated best by relating some personal experiences of the author.

During the decade between 1930 and 1940, the author practiced in a rural southern Minnesota community and participated in the care of five patients who had suffered from impalement of the rectum and perforation of the colon. All of these injuries occurred when the patients jumped from a hayloft onto a load of hay, with the handle of a pitchfork entering the rectum. All five patients succumbed from generalized peritonitis within ten days following the injury. Only one patient had surgery, and in this case a colostomy was performed. The other four patients were treated with intravenous fluids and morphine. The sulfa drugs and antibiotics were not yet available. In this small series, the mortality rate was 100%.

Between 1940 and 1960, the author again participated in the care of six perforations which were sustained during sigmoidoscopic examinations in hospitals associated with the University of Minnesota, one patient sustaining the perforation during sigmoidoscopy under general anesthesia with the others occurring in elderly individuals being sigmoidoscoped in the cancer detection center or in other hospitals. All were operated upon within a period of two or three hours after the perforation had occurred. The perforations were closed and no colostomies were performed. There were no serious complications and no deaths. The average hospital stay was seven days after surgery. Statistically, this group represents far too small a number for any definitive generalizations. Nevertheless, this experience in the surgical practice of one individual indicates the progress which has been made in the past two decades.

It is unfortunate that iatrogenic factors continue to harass those who are in charge of train-

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William C. Bernstein *is clinical professor of surgery and director, Division of Proctology, University of Minnesota, Minneapolis.*

ing programs in proctosigmoidoscopy. Sincere but eager residents, in their overenthusiastic attempts to do complete examinations, satisfactory biopsies, and thorough coagulation of polyps in the sigmoid, are involved in many of the perforations which occur in clinics and operating rooms. In drawing attention to the innocent transgressions of the overzealous resident, we must never forget that the most experienced operator is not immune, despite the best facilities and the exercise of the most prudent precautions and safety measures. There are few men who, after many years' experience in proctosigmoidoscopy, have not seen the small intestine through the proctoscope.

Perforations of the rectum and colon fall into one of several categories which may be outlined as follows:

1] Objects introduced from above
   - Gunshot wounds
   - Stab wounds
   - Swallowed objects
   - Colostomy irrigating tips

2] Blunt trauma to the abdomen
   - External blows sustained in automobile and airplane accidents
   - Blows, bumps, falls, and crushing injuries

3] Spontaneous rupture of the colon

4] Objects introduced from below
   - Enema tips
   - Proctoscopes
   - Clinical thermometers
   - Impalement on pitchfork handles and hard objects protruding from the ground, tree twigs, mechanical devices, and so on

5] Violent increase in intraluminal pressure
   - Compressed air injuries
   - Explosions during fulguration of polyps
   - Barium enema X-ray examinations

6] Perforations due to extensive fulguration of polyps

7] Biopsy forceps injuries

8] Perforations occurring during surgery on other organs, that is, prostate, uterus, vagina, and so on

9] Perforations due to intrinsic colon disease
   - Neoplasms
   - Inflammatory disease
     - Diverticulitis
     - Ulcerative colitis
     - Amebiasis
     - Pneumotosis cystoides intestinalis

Some of the more unusual perforations of the colon deserve special comment. One unfortunate example is the perforation occurring during the barium X-ray examination. These accidents are most distressing and are being reported in increasing numbers. Santulli[2] has stated that perforations occurring during the barium enema examination and resulting in barium being diffused through the peritoneal cavity carry a mortality of over 50%. Barium sulfate produces a highly fatal type of peritonitis and, if a perforation is suspected following the X-ray examination, the abdomen should be opened with dispatch and the perforation closed in the usual manner. The barium should be removed by lavage. During the past year, a perforation of the colon occurred during the preparation for a barium enema. Castor oil was administered and the bowel perforated just proximal to an obstructing carcinoma.

Another infrequent and unusual colon perforation is caused by the spontaneous rupture of the colon without clinical evidence of organic pathology. This rare type of perforation has been reported from time to time. DeMuth[3] in 1960 stated that no cases of spontaneous rupture of the colon have been reported in females or in children. Males without hernias rarely suffer from a spontaneous rupture of the colon. DeMuth reported one such case with recovery. The author had a case of spontaneous rupture of the transverse colon in a patient suffering from cardiac decompensation. A laparotomy was performed, and the abdomen was found to be full of liquid feces. The patient expired on the day of surgery.

Still another unusual type of colon perforation results from an injury caused by compressed air. Occasionally, a prankster, usually around a filling station, releases compressed air under high pressure near the anal opening. Because of the funnel-shaped arrangement of the anatomy, the air rushes into the colon under high pressure and produces a laceration which is usually present on the left side. This type of injury must be suspected whenever there is evidence of horseplay involving access to compressed air equipment.

Another and most distressing type of perforation is the explosion occurring during the fulguration of polyps of the rectum or sigmoid. This is always a serious situation and it is important that X-rays of the abdomen be taken to determine whether or not free air is present under the diaphragm. Abdominal exploration is indicated if there is evidence of perforation.

Wyesundera and de Silva[4] reported seven fatal cases of colon perforation due to Entamoeba histolytica.

When properly treated, colon perforations without any other visceral injuries have a mortality of about 6%. Imes[5] pointed this out in 1945, with the observation that if other organs were injured the mortality rose to over 40%. In 1963, Saunders[6] discovered that intraperitoneal perforations of the colon were best treated by primary suture of the perforation and that when other procedures, such as primary closure with a diverting colostomy, exteriorization, resection with a colostomy, or resection with primary anastomosis, were performed both morbidity and mortality increased substantially. Morbidity and mortality rates are higher also in patients in the older age group.

At the Minneapolis General Hospital,[7] there were 40 penetrating wounds of the abdomen treated between 1955 and 1960. There was an overall mortality of 17.5%. Stab wounds had a mortality of only 5.5%. Pistol wounds had an overall mortality of 12.5%, and shotgun wounds carried an overall mortality of 66.6%. These figures indicate quite clearly that the relatively simple wound from a bullet or sharp instrument is much less dangerous than the shotgun wound with its extensive internal destruction of tissue and involvement of other organs and structures.

Because successful handling of cases of perforation of the colon depends so much upon early diagnosis and prompt treatment, emphasis must be placed upon these points. It is well to point out, however, that the diagnosis of a perforation is not usually difficult if the surgeon has a high enough index of suspicion. If the injury is from without, the wound is obvious. In those cases where no external wounds are apparent, the history usually suggests the possibility of a colon perforation. Physical findings of the abdomen, plus positive X-ray evidence of free gas under the diaphragm, leave little doubt as to the diagnosis. Exploratory laparotomy should be carried out as rapidly as is consistent with good preoperative preparation. Where there is a question of massive internal hemorrhage, surgery should be carried out even though the patient is in shock. Blood substitutes and other intravenous fluids can be used until whole blood can be started. Waiting to replace blood volume or to correct shock before surgery is started may cost the patient his one chance of recovery. Bleeding from large vessels must be controlled in order to reverse the morbid process.

When the abdomen is opened in suspected cases of perforation due to knife or gunshot wounds the surgeon must be alert to the possibility of multiple perforations and injuries to other organs. Bullet wounds of the intestines are rarely single and are usually present in multiples of two. Injuries to the liver, spleen, pancreas, stomach, kidneys, bladder, and large vessels often occur at the time of the accident and add greatly to the problems of the surgeon and to the gravity of the situation.

Simple perforations of the colon can usually be closed with a two-layer closure. A diverting or proximal colostomy is not necessary unless there is gross contamination with stool or barium or there is evidence of active peritonitis. For badly lacerated wounds of the colon, segmental resection may be the operation of choice. Here, again, the indications for doing a complementary colostomy remain the same.

Personal experience has shown that most colon injuries in civilians can be satisfactorily handled by primary repair. A colostomy is usually not necessary because tissue destruction is far less than in those injuries caused by battle wounds. This means that exteriorization is not essential, is less satisfactory, and is seldom performed today. Resection is indicated for severely damaged intestinal segments, with continuity being reestablished by end-to-end anastomosis. When the patient's condition is extremely critical and prolonged surgery is out of the question, exteriorization should be considered. Irrigation of the abdomen with solutions of antibiotics is used by many surgeons. Thorough lavage with saline to remove all foreign material is probably as effective as the former method.

In perforations of the rectum, one of the problems of diagnosis is that often there are no particularly dramatic symptoms. Perforation of the bowel wall does not often produce pain; however, the spilling of enema fluid, fecal matter, or blood into the peritoneal cavity may cause symptoms of abdominal pain or discomfort. This eventually results in the classic signs of peritoneal irritation. Rectal perforations do not often produce marked symptoms of shock, and the bleeding which occurs usually ceases spontaneously.

Once the diagnosis of a perforation of the rectum is made, it is imperative to determine whether the peritoneal cavity has been entered and whether or not the bladder is involved in the injury. Cystoscopy and cystograms are most helpful. In many cases, the perforation may be palpated with the examining finger or visualized through the proctoscope. A flat and upright X-ray of the abdomen may reveal evidence of free intraperitoneal air. A barium enema examination should not be done. Perforations occurring low in the rectum and not involving the peritoneal cavity or bladder are best treated conservatively. Extensive perforations and those involving the peritoneal cavity or bladder should have a diverting colostomy performed. Perirectal surgical spaces need not be opened unless definite evidence of infection in the space is present. Debridement, antibiotics, and supportive measures will suffice in most cases of rectal injuries.

SUMMARY AND CONCLUSIONS

Untreated traumatic perforations of the colon are usually fatal. Colon perforations are much more frequent during military combat than in civilian practice. Perforations of the colon sustained during combat are usually much more serious than those occurring in civilian life. In the past two decades, the mortality rate of colon perforations has dropped markedly due to improved surgical techniques, chemotherapeutic agents, and antibiotics. Improved anesthesia and blood replacements share in this improvement record. Perforations involving more than one organ and perforations occurring in older-age patients carry a much higher mortality rate. Early diagnosis and prompt treatment assure the best recovery rates. Although these injuries are relatively rare in civilian practice, physicians must always keep the possibility of a colon perforation in mind if there is any reason to suspect injury to the abdomen or its contents. Primary closure of the perforation without colostomy is the procedure of choice in simple perforation. Bowel resections, exteriorization procedures, and multiple injuries carry much higher morbidity and mortality rates. A complementary colostomy should be done if peritonitis is present or if gross contamination of the peritoneal cavity has occurred. Rectal perforations not complicated by bladder or peritoneal involvement are best treated by conservative measures.

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Vascular Trauma—Max E. Harris, M.D.

(Continued from page 307)

SUMMARY

Care of the injured patient requires some knowledge of vascular surgery. Relatively recent advances have made possible a more ideal method of therapy and in many cases a more satisfying end result. Some aspects of peripheral vascular surgery and illustrative case reports have been presented.

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Extremity Fractures in the Patient with Multiple Injuries

FRANK S. BABB, M.D., WAYNE W. THOMPSON, M.D.,
and ROBERT B. WINTER, M.D.

St. Paul

THE ESSENCE of good care of extremity fractures in the patient with multiple injuries is in proper evaluation of the extremity injuries and proper timing of the treatment to coincide with the treatment being given for the other injuries. It is, therefore, essential to have a thorough and complete evaluation of the extremities at the time the patient is originally seen. A list of these injuries must then be made and a logical approach taken for each. The approach to these injuries must be tempered by the general condition of the patient and by the specific injuries he has received in other areas of his body. It is a cooperative enterprise carried out with the general surgeon, thoracic surgeon, neurosurgeon, and urologist all taking their roles in a team attack. With any team there must, of course, be a captain. Who this will be depends upon the nature of the patient's problems, who has seen him first, and what the local situation is, but it is important to have one person in charge. Once the immediate evaluation has been made, a planned approach to the entire patient should be initiated and a priority established for treatment of the injuries.

EVALUATION OF THE EXTREMITIES

Evaluation of a traumatic injury to any extremity involves examination of the circulation, the sensation, the skin, the skeleton, and the musculotendinous apparatus. It is just as important to evaluate all these things in a severely injured person as in any other person. Oversights are frequently made in evaluating the extremities because of other injuries distracting attention elsewhere. The circulation is, of course, the most important vital function to be evaluated. This includes examination of pulses, skin temperature, blanching, and sensation. Examination of nerve function involves testing for both motor and sensory components. Even a partially comatose individual will respond to painful stimuli, and a gross examination of major nerves can readily be performed. Simply the position of the extremity can give clues as to the function and integrity of various nerves and tendons. It is also important to evaluate the skin and to look for any open wounds which may or may not communicate with tendons, nerves, or fractures. Examination for fractures will include gross deformities, crepitation, pain, tenderness, and function. Examination for tendon injuries includes observation of the attitude of the extremity and the ability to move various portions of it, since some major tendon and muscle injuries can be detected by direct palpation of the defect.

EMERGENCY CARE OF THE EXTREMITY

After evaluation has been performed, an open wound should be covered with a sterile dressing, a large, bulky padded dressing applied, and a plaster or metallic splint applied over this. This splint and dressing then serve to protect the wound and the extremity while the patient is undergoing other examinations and treatment, depending on his general condition. The multiply-injured patient often requires tracheotomy, insertion of chest catheters, other X-ray examination, catheterization of the bladder, cutdowns, and other procedures which can absorb one or more hours of time, during which period the fractures must be adequately stabilized. Stabilization of the fractured extremity will, in itself, help in stabilizing the general condition of the patient. Excessive motion causes further bleeding and pain, both of which serve to increase and aggravate the poor condition of the patient.

FRANK S. BABB, M.D., *is assistant clinical professor of orthopedic surgery,* WAYNE W. THOMPSON, M.D., *is clinical instructor, Division of Orthopedic Surgery, and* ROBERT B. WINTER, M.D., *is clinical instructor, Division of Orthopedic Surgery, University of Minnesota, Minneapolis.*

Open fractures. Except for vascular injuries in extremities, open fractures demand the top priority. However, their care may have to be delayed by treatment of even more life-threatening problems such as flail chest, intracranial hemorrhage, or severe abdominal bleeding. At the earliest possible opportunity, and certainly within the first ten to twelve hours, the patient must be taken to the operating room where the wounds must be thoroughly irrigated, thoroughly debrided, the fracture reduced, the skin closed, and a cast or traction applied. Of second importance are skin injuries without communication to the fracture. These also must be irrigated, debrided, and closed before infection has had time to occur. Any infected extremity will, of course, be impossible to reconstruct at a later date.

Closed fractures. Closed fractures do not constitute any emergency unless there is injury to nerves or major vessels. Any dislocation must be reduced, but a majority of fractures can be simply splinted without attempting a reduction, and definitive treatment can be delayed for several days if necessary.

Vascular injury with fractures. Recent statistical evidence indicates that fractures of the long bones, such as the femur, humerus, radius, and ulna, will heal faster with an open reduction if the open reduction is delayed until ten to twenty days from the time of the injury. It appears that surgical interruption of the healing process at this time stimulates further healing. The total time of healing is much reduced despite the initial delay. Therefore, a fracture, for example, of the midshaft of the femur is best delayed for ten to twenty days if it requires internal fixation and if there is no need for emergency internal fixation. The exception would be for those indications requiring immediate fixation, such as vascular or nerve injury.

Nerve injuries. Injuries to the nerves in an extremity may occur as the result of a fracture or as the result of contusion or laceration. If there is an open wound it is important that the wound be adequately debrided as described above and good skin coverage be obtained. In a decision to repair nerves in patients with multiple injuries, it is wise not to attempt any definitive repair of a nerve. There is no harm in waiting until the nerve repair can be scheduled as an elective procedure. Hastily attempted nerve repair under less than ideal conditions is rarely successful. However, during the process of wound debridement, it is wise to tack the ends of the nerve together so they will not retract, and this will make definitive nerve repair easier at a later date. "Tagging" of the nerve ends is unnecessary. It is much more important to bring the ends together by one or two stitches to prevent retraction than it is to identify them, as they are not difficult to find at a later date.

Tendon injuries. Tendon injuries are usually caused by an external lacerating object rather than by fracture fragments. Some internal injuries are best treated at the time of the original injury and others should be left until a later date. These will be discussed further, later in the article.

SPECIFIC INJURIES

Pelvis. Injuries of the pelvis are very frequent in the multiply-injured patient. The first consideration must be given to the bladder and urinary tract. A urine specimen must be obtained and a Foley catheter inserted. The multiply-injured person almost always requires an indwelling catheter and one is almost routinely indicated in such a patient. If there is any bleeding, an emergency cystogram should be obtained. Urologic consultation is indicated if there appears to be any possible injury to the bladder, urethra, ureters, or kidneys. The loss of large volumes of blood can also be expected from an injury to the bony pelvis. The patient can rapidly exsanguinate unless this factor is kept in mind. Adequate blood replacement is the primary treatment. On rare occasions, ligation of the internal iliac artery may be indicated.

Hip joint dislocations. These must be reduced quickly, preferably within six hours and certainly within twelve hours of the time of the injury. The longer a hip is left dislocated the more serious the complication of avascular necrosis of the femoral head. Spinal anesthetic or a very brief inhalation anesthetic will allow reduction of the hip. Usually the multiply-injured patient requires an anesthetic for treatment of this or other injuries and the dislocation can be reduced at that time. A dislocated hip cannot be left until a later date. Fractures of the hip, both intracapsular and extracapsular, should be treated by traction using a Steinmann pin in the proximal tibia or distal femur. There is no indication for emergency hip nailing in the multiply-injured patient.

Femur. Emergency treatment of fracture of the femur is primarily the institution of balanced skeletal traction with a heavy Steinmann pin in the proximal tibia or the distal femur. Open fractures should be debrided, irrigated, and closed. Internal fixation of these fractures as an emergency by either intramedullary nail or plating is not indicated except for the single indication of vascular injury simultaneous with the femur fracture. Skeletal traction should always be used; skin traction is insufficient in the multiply-injured patient.

Knee. Open wounds of the knee are frequent and the important thing is to irrigate and close the joint as soon as conceivably possible. This is usually done at the time the patient is receiving general anesthetic for other procedures. If the skin is not open, fractures about the knee should be treated by cast or traction. Any internal fixation can be delayed until the patient's condition stabilizes.

Fractures of the tibia. These are the most frequently seen extremity fractures in the multiply-injured patient. They are most often open and the critical point is to obtain a clean closed wound by careful irrigation, debridement, closure of the wound, and immobilization of the extremity in a plaster cast. Even a definitive reduction can be obtained at a later date. There is almost no indication for the insertion of pins, nails, bolts, or screws in the tibia under such circumstances. Traction should also be avoided in fractures of the tibia.

Ankle. Open wounds should have irrigation, debridement, closure, and a cast. In a temporary reduction, a definitive reduction can be performed at a later date if necessary. Some open fractures can quickly be reduced with a Kirschner wire or a threaded pin which will save a second operation at a later date. In general, it is unwise to attempt any internal fixation on an emergency basis.

Foot. Again, open wounds should be closed, tendon injuries should be repaired, nerve injuries should not be repaired, and a cast should be applied.

Humerus. Careful attention must be directed toward the neurologic status and the vascular status. Radial nerve injuries are very common and are usually missed. Because of concomitant injuries to the abdomen and chest, it is rarely possible to immobilize the humerus by bandaging it to the chest. Hanging casts are equally unsuccessful because the patient is almost always lying flat. For this reason, traction with a skeletal pin through the proximal ulna is usually the treatment of choice. Open reduction and internal fixation of the humerus are necessary on certain occasions. These are best delayed until ten to twenty days following injury and, for this reason, need not be done on an emergency basis unless there is injury to the brachial artery.

Elbow. Again, closure of open wounds of the joint is of the utmost importance. Minor fractures can quickly be pinned while the wound is open. Many injuries can be treated by traction as described above for the humerus. Excision of the radial head should be performed at the time of the initial treatment. Fractures about the elbow do not do well with delayed treatment, and it is best to attempt to get as much done at the initial procedure as is possible. This is the one area where internal fixation and insertion of various metallic devices are indicated on an emergency basis at the time of the initial treatment in order to preserve function of the joint.

Forearm. Open wounds should, of course, be irrigated, debrided, closed, and a cast applied. Definitive reduction can await a later date. If open reduction is necessary, and it very frequently is for fractures of the shaft of the radius and ulna, this is best performed at a later date.

Wrist. Wrist fractures are best treated by simple reduction and splinting. Since these can be performed with regional block anesthetics, there is little problem in treating these injuries. One must be observant for injuries to the median and ulnar nerves.

Hand. Reconstructive procedures of the hand cannot be performed if there is inadequate skin coverage or an infected wound. Therefore, the major consideration given to the emergency treatment of hand injuries must be the obtaining of adequate and complete skin coverage as quickly as possible. A badly injured hand in the multiply-injured patient should have whatever is necessary to obtain good skin coverage, and the hand should be splinted in the position of function. All tendon injuries can be repaired at a later date. Flexion tendon injuries should never be repaired primarily under these circumstances. Extensor tendons can be brought together quickly with a suture at the time the skin wound is being closed and heal well with simple treatment. If there are open wounds, fractures can often be quickly pinned without delay in time and, if so, this is advantageous.

INJURIES OF THE SPINE

Although this does not fall within the general topic of injuries to the extremities, in the multiply-injured patient it does fall within the domain of the orthopedist involved in treating the extremity injuries and, therefore, we believe merits discussion at this time. Fractures of the spine are almost never open fractures. Fractures must be categorized as to whether they are stable or unstable and whether there is neurologic damage or not. Stable fractures without neurologic involvement do not demand much treatment. Simple bed rest is all that is necessary, and this is obviously being done for the other injuries. Unstable fractures, and these usually have neurologic damage, constitute another problem entirely.

The complete neurologic loss at the level of the fracture at the time of the injury and thereafter is usually an irretrievable injury, and surgical procedure directed to the spinal cord is unnecessary.

An incomplete lesion and one that is progressing to a worse condition neurologically constitute an emergency and open surgery is necessary. It is important both to decompress the contents of the neural canal and to establish stability. All too frequently the spine is decompressed, only to have re-injury to the spinal cord because of shifting of the fracture fragments. A decision to operate on the spine fracture in the face of other injuries to the head, chest, or abdomen, for example, constitutes an extremely difficult judgment and each case must be taken on its own merit.

COMMON ERRORS

Vascular diagnosis. Failure to diagnose vascular injuries is almost always the result of inadequate physical examination at the time of the first assessment of the patient's injuries. If a vascular injury is associated with a fracture, reduction of the fracture should be obtained quickly to see if the circulation improves. If the circulation is not restored by reduction of the fracture, then open surgical exploration of the artery in the area of the fracture is mandatory. Arteriography may sometimes be helpful but it is often a serious waste of time before surgery, as valuable time may be lost obtaining a blood supply to the extremity. Arteriograms can be obtained on the table with the artery exposed and this is a preferable choice to preoperative arteriography except in certain cases.

Diagnosis of nerve injuries. Again, this is a failure to adequately examine the extremity. A comatose patient is difficult to examine and often one can only go on the response to stimulation. In the completely comatose patient, sometimes it is impossible to adequately determine the neurologic status, but repeat neurologic examination should be performed as the patient's sensorium clears.

Diagnosis of fractures. This usually occurs in two areas. First, in the comatose patient who cannot tell the examiner where he hurts, it is important to palpate adequately every bone in every extremity, plus the spine, to feel for swelling, crepitation, or other signs of injury. Many X-rays are usually necessary to be sure the fractures are not missed. Fractures that are frequently missed are those where there are two fractures in the same bone. Second, probably the most commonly missed is a fracture of the hip where there is a fracture of the femur on the same side. We therefore have a rule in our hospitals that any patient with a fractured femur must have X-rays demonstrating the entire length of the bone to be sure there is no missed hip fracture or dislocation.

Emergency treatment. Another common error is the failure to treat adequately the extremity as part of the emergency treatment. We have discussed above the fact that stabilization of fractures by cast or splint helps to diminish pain. It also diminishes the hemorrhage and, therefore, allows stabilization of the patient's general condition.

Open fractures. A major area of error is in the often inadequate and neglectful treatment of open fractures, which leads to infection and virtual impossibility of later reconstructive procedures because of the infection. The important thing in treating open fractures is to obtain a clean closed wound. It is not so important to obtain a beautiful reduction at the time of the initial treatment.

SUMMARY

Fractures of the extremities in the multiply-injured patient rarely constitute an impossible situation. It is almost always feasible to provide good treatment of the extremity, regardless of the general condition of the patient. There is no excuse for inadequate therapy just because the patient has severe injuries to other portions of his anatomy. Most errors in treatment can be avoided by a carefully performed, comprehensive examination at the time of the injury, combined with a systematic logical plan of attack on a teamwork basis.

The Early Treatment of Major Burns

JAMES W. LA FAVE, M.D.

Successful resuscitation and management of a patient suffering major burns has always been a formidable clinical undertaking.

Formerly, the prognosis for patients suffering extensive burns was poor. But today, if adequately managed in the shock phase, the prognosis has never been more promising. This is true because of the dramatic success of topically applied sulfamyelon ointment and 0.5% silver nitrate packs. Their use has demonstrated the effectiveness of locally applied agents in control of burn wound sepsis and has greatly reduced not only the morbidity but the mortality of extensive thermal burns.[1,2] In this light, Underhill's statement made thirty-five years ago is, if anything, more pertinent today: "It is of little value to make a perfect dressing and allow the patient to die from shock."[3]

The following general procedures of management are employed by the surgical staff and house officers at the St. Paul–Ramsey County Hospital.

The initial examination must determine the need for emergency tracheostomy, for on rare occasions establishment of an airway is an immediate and urgent lifesaving requirement.

A history of the agent and mode of burning orient the physician to the severity of the thermal exposure. Flame burns, especially those that ignite clothing, are usually most severe. Scalds are frequently less severe, but boiling tar, grease, chocolate, or molten metal are notable exceptions. Contact, chemical, and electrical burns may cause extensive tissue destruction.

All the clothing is removed. The burned area is initially estimated by the rule of nines, and, when time permits, depth and area of burn should be charted in detail. The data provided by Lund and Browder[4] or vonMeeh[5] accurately map body area for various age groups. At this juncture, estimation of burn depth is tentative.

Next, the patient is weighed and a venous cutdown is secured. When possible, we like to do this on a basilic vein, inserting a large-bore polyethylene catheter. This is threaded proximally and serves not only for the administration of fluids but also for monitoring the central venous pressure. Blood for base line studies, complete blood count, hematocrit, electrolytes, and plasma hemoglobin is drawn. A Foley catheter is placed in the urinary bladder, and the first collection of urine is sent to the laboratory for routine analyses and measurement of the hemoglobin concentration. Urine volumes and specific gravity are measured hourly on the ward.

SHOCK

Controversy exists as to the ideal resuscitative solution in the treatment of burn shock. We prefer lactated Ringer's solution and believe the efficacy of such a physiological saline solution is established on the basis of well-founded experimental and clinical studies.[6-14] Unless there is need to replace known blood loss, the administration of blood in the early postburn period is deferred. The use of blood during this time has been associated with high incidence of pulmonary congestion and edema.[10] The colloidal osmotic effect of plasma does not greatly influence shock mortality. As a resuscitative fluid, it is no more effective than saline,[12] and the risk of serum hepatitis always attends its use. Plasma expanders fail to meet the standards of safety and effectiveness which are achieved with saline. Although a beneficial effect has been attributed to the anticoagulative properties of dextran solutions, red-cell slugging has not been demonstrated in burn patients except in the special situation of the bulbar conjunctiva.[15]

Shock results from the physiological consequences attendant upon loss of sodium-containing extracellular fluid into the burn wound.[3,9,10,13] Treatment must be directed to the rapid restoration of this sodium and water loss. Lactated Ringer's solution does this without producing metabolic acidosis, which may occur if large volumes of saline are infused (sodium and chlorine concentration, 155 mEq. per liter). Moyer recommends that lactated Ringer's solution be infused at a rate sufficient to maintain

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JAMES W. LA FAVE *is from the department of surgery, St. Paul–Ramsey Hospital, St. Paul.*

[1] blood pressure and pulse rate within normal range, [2] a urine flow of 25 cc. per hour, and [3] normal mental status. Venous pressure is monitored and, if it rises to over 10 cm. of water, the infusion rate is slowed.[13] Reweighing the patient twice daily accurately establishes the amount of fluid retention. Gains of 10 to 20% of body weight are not uncommon during the first two days.[13] It has been stressed that, even with the above criteria satisfied, the red blood cell concentration often will continue to rise. This is ignored in adjusting the infusion rate.[13] Severely burned patients may require 10 to 20 liters of Ringer's solution per day during the first two postburn days. These patients are digitalized because this sequestered fluid is mobilized and excreted during the diuretic phase which occurs shortly after the first forty-eight-hour postburn period. Should hemoglobinuria occur during the early postburn period, a total of 25 to 50 gm. of mannitol is administered over twelve to twenty-four hours in the lactated Ringer's infusion. Safe and satisfactory resuscitation is obtained by titration of the patient's clinical response, mental status, blood pressure, pulse rate, urine volume, and venous pressure with the lactated Ringer's infusion. No reliance is placed on formulas to gauge the infusion rate or volume.

Acute gastric dilatation may be a cause of refractory hypotension, and it must be recognized and treated promptly with a nasogastric tube. Yet, this occurs infrequently. These patients are thirsty, and many can safely ingest large quantities of oral electrolyte solution. A cold solution containing 4.5 gm. sodium chloride and 1.5 gm. sodium bicarbonate per liter is offered, and the patients are checked frequently for gastric dilatation. If this is tolerated, shock phase losses frequently can be compensated for almost exclusively in this manner. This is a consideration of great importance in the mass casualty situation. In our experience, reliance on oral and intravenous electrolyte solutions has proved to be most satisfactory. Plasma is administered in only two rather special situations: [1] where starvation and total protein depletion may have preceded the burn[10] and [2] extensively burned children under two years of age receive 0.5 cc. of plasma (per kilo, per percent degree burn) because its antibody content favorably influences shock phase and late mortality in this group.[16] Renal failure has yet to occur in our experience. This general regimen has proved to be safe and effective.

RESPIRATION

Respiratory insufficiency is the most common cause of death during the early postburn period.[17] Omitting blood and plasma and prophylactic digitalization may well reduce the incidence of pulmonary congestion and edema. Placing all severely burned patients on a Stryker frame or circular bed facilitates frequent change of position, and this reduces the incidence of hypostatic pneumonia. However, the most serious cause of respiratory damage associated with burns is the inhalation of incomplete products of combustion or noxious gases.[18] (Air has a low heat capacity and seldom causes respiratory tract damage.) This is commonly associated with burns about the face and neck incurred in a closed space.

Respiratory mucous membrane damage induces hyperemia, edema, exudation, and, when severe, necrosis followed by slough. Symptoms include: dyspnea, tachypnea, progressive hoarseness, inspiratory wheeze, cyanosis, and, as anoxia progresses, excitation progressing to delirium. Any or all of these symptoms may be present initially or follow a symptom-free interval.

The relative paucity of X-ray findings may be in marked contrast to the clinical difficulty. Linear areas of atelectasis, with or without areas of compensatory emphysema, often constitute the only roentgenographic findings.

Upper airway obstruction is an indication for immediate tracheostomy. More often, the problem lies further down in the respiratory tree as edema, bronchospasm, and exudation compromise the small bronchial lumens. Obvious respiratory difficulty, especially that associated with wheezes and cyanosis, also dictates a compelling need for tracheostomy. It is best performed early before edema distorts the local anatomy; it may have to be performed through burned tissue. If symptoms are less severe, one may choose to delay tracheostomy. This is permissible, but a tracheostomy set is maintained at the bedside, for it may be needed as late as the fourth to the sixth postburn day, when slough and expectoration of the mucous membrane ensue.

Steroids are indicated to reduce the respiratory inflammatory response. Parenteral administration of prednisone, 4 mg. per kilogram, is commonly employed. Should tracheostomy be necessary, a cuffed tube is inserted. Intermittent positive-pressure ventilation then can be accomplished by hand, employing an anesthetic gas machine, or with a mechanical respirator. With the patient well oxygenated, the tracheobronchial tree is lavaged with 100 cc. of sterile normal saline containing 100 mg. of hydrocortisone succinate (Solu-Cortef®) and one million units of aqueous penicillin. This is immediately removed with a suction catheter, and respiratory assistance is resumed. Warm water, midstream nebulization is important, especially if continuous respiratory support is necessary, to prevent drying of the already damaged respiratory mucosa. Tracheobronchial toilet must be a continuous concern, for pneumonitis will rapidly occur behind obstructed bronchi. Suction is carefully performed by a masked attendant who wears sterile rubber gloves and employs a sterile catheter. Bronchospasm may be most difficult to control and requires aminophylline and isoproterenol (Isuprel®) in addition to the above measures. While the patient is on steroids, antacids are given to prevent acid-peptic ulceration of the upper gastrointestinal tract.

WOUND

After treatment of shock has been instituted and the respiratory status is stabilized, attention is directed to the wound itself. A single, 8-mg. intravenous infusion of morphine sulfate provides adequate analgesia for adults. The intravenous route is preferred because of the often-delayed absorption from subcutaneous injection sites. Burn patients require little analgesia beyond that which is needed to clean the wound. It is well to guard against oversedation.

Using sterile instruments, all loose and blistered skin is removed. Multiple cultures are taken. The wounds are then washed with hexachlorophene soap (pHisoHex®) and sterile saline. All this is readily accomplished on the ward. Grease or medication must be completely removed, and this is sometimes facilitated by placing the patient in a Hubbard tank or tub filled with normal saline. The wounds are now ready for application of sulfamylon cream (not yet available commercially) or 0.5% silver nitrate dressings. Once in the silver nitrate dressings, the patient experiences little discomfort from his wounds. However, with these hypotonic packs in place, electrolytes must be checked every six to twelve hours in adults and as often as every three to four hours in children. This is necessary until oral alimentation is established—usually at forty-eight hours—and large electrolyte supplements can be ingested. Such precautions are essential to prevent undetected onset of acute hyponatremia because body electrolytes, particularly sodium, readily diffuse out through thermally damaged epithelium into these hypotonic packs.[2]

All patients are given tetanus prophylaxis in the amount of 0.5 cc. of tetanus toxoid. Those who have not had active immunization or booster shots within the last seven years receive hyperimmune human antitetanic serum. Rapid, active immunization is begun, and 0.5 cc. of toxoid is administered each week for three weeks. Penicillin is administered orally or parenterally if no sensitivity exists to insure against lymphatic invasion by gram-positive cocci.

SUMMARY

This discussion has dealt with the emergency care of the extensively burned patient during the shock phase. Major burns are catastrophic injuries that formerly exacted a high mortality. However, the present era of burn therapy is the most exciting in decades. Although much remains to be learned about the mechanism of the tremendous fluid and electrolyte shifts and alterations in respiratory physiology induced by burns, most of these are amenable to basic therapeutic maneuvers. Once through the shock phase, given effective local measures, the severely burned patient has a more hopeful prognosis.

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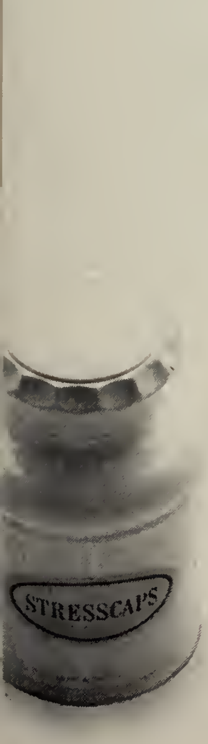

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Book Reviews . . .

Immediate Care and Transport of the Injured

edited by GEORGE J. CURRY, M.D., *187 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $7.50*

Immediate Care and Transport of the Injured is a manual compiled by Dr. George J. Curry containing chapters by twenty-one individuals considered expert in their respective fields. The manual is designed for both medical and paramedical personnel and contains a large variety of valuable information. It deals not only with specific emergency situations but also with general policies and information regarding the conduct of satisfactory emergency care and transportation facilities. The topics covered include such items as the ambulance, laws and ordinances pertaining to emergency medical care, mass casualty management, and hospital emergency room facilities.

Specific first aid and medical management information is also included. The topics covered include respiratory and cardiac arrest, diving injuries, athletic injuries, industrial injuries, and burns.

The entire book is a reflection of many medical experts in the field of injuries. As such, it puts forth each author's philosophy toward the management of his particular field of medical emergency. The reflections, based on vast experiences, provide the less experienced physician and paramedical personnel with a sound background of information on all fields of trauma in emergency medical treatment.

Dr. Curry's chapter, "The Ambulance," is particularly well written and thought provoking. Such topics as ambulance attendant qualifications, the speeding ambulance, and siren use and abuse are covered.

THEODORE A. PETERSON, M.D.
Minneapolis

First Aid for Emergency Crews

by CARL B. JOUNG, JR., *165 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $4.50*

First Aid for Emergency Crews is a 160-page manual written for ambulance crews, law enforcement officers, fire service personnel, industrial nurses, and any other lay personnel dealing with first aid and transportation of the injured. Its easy reading prose and illustrative and captivating line drawings should prove effective in maintaining a high level of interest throughout the entire book. The book covers all facets of emergency care, from examination of the accident scene through phases of emergency first aid and transportation of a large variety of commonly encountered injuries and medical emergencies. Sections on public relations, legal implications, and care of the dead are also included.

A prominent feature of this manual is the careful attention to the principles of the psychology of injuries and medical emergency situations. In addition, principles of advanced first aid are very clearly illustrated.

This is not a manual for beginning first aid instruction but rather for advanced students of first aid in emergency transportation of the injured.

THEODORE A. PETERSON, M.D.
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(Continued on page 14A)

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(Continued from page 12A)

Comparative Basic Cardiology

by JANE SANDS ROBB, M.D., *602 pp., ill., Grune & Stratton, New York, 1965. $39*

Jane Sands Robb has gathered a tremendous amount of information over a period of years and produced this monumental work on comparative basic cardiology. As her interests in her earlier years widened, she must have become increasingly aware of the difficulty in locating information concerning hearts, and decided to do something about it. In no other volume is there available, at present, this wealth of information as to the comparative gross anatomy, microscopic anatomy, embryology, electron-microscopy, histochemistry, and electrophysiology of the heart of so many species of animals. It is obvious that no one person could have firsthand knowledge of all these varieties of information even for the heart of one species. She, therefore, set for herself the task of reviewing the literature and tabulating the references. There seemed no better way to organize the material than to employ standard classifications of animals and enter the information at the appropriate places.

She chose to make direct quotations from the literature in the interest of accuracy, freedom from bias, and variety of style. She indicates what is known and what is not known, with the hope of stimulating some scientists to fill the gaps and inspiring some young investigators to carry on the project. She points out that the background for a beginning researcher is to know what has been done, who has done it, what methods were available, and what newer methods might provide further information. She quotes obsolete methods and points out that improved methods have changed conclusions and, in order to emphasize the fact, that progress has been made and furthermore that an established truth is not necessarily established for all times.

Dr. Sands techniques and teaching methods should intrigue the curiosity of the young investigator and demonstrate how information has been gathered and been presented through the years. She has succeeded in accomplishing what she set out to do; she has submerged her own work and made it all an interesting part of the whole. The volume has been profusely illustrated with 528 figures, 67 in color on the last 40 pages. The format is excellent.

The work should be interesting and stimulating to not only the anatomist, histologist, embryologist, and cardiologist, but also to the pediatrician and cardiac surgeon in their study of congenital heart lesions. The lesions are related not only to the ontogeny of the individual species as man, but also to the phylogeny of the race or group of animals as well. The congenital lesion depends upon the stage of development of the heart and vascular system, at which the processes are arrested in the embryo.

The volume should also interest the electrocardiographer to whom the development of the specialized conduction system of the heart is of great concern.

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GEORGE R. HERRMANN, M.D., PH.D.
Galveston, Texas

The Burn Wound

by CAPT. STANLEY E. ORDER, M.D., *and* COL. JOHN A. MONCRIEF, M.D., *72 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $7.75*

The authors present an excellent thesis which focuses its primary attention upon the burn wound rather than the disturbed physiology of the other body organs as is usually presented. It is now clear that the burn patient initially can be kept alive by careful attention to electrolyte balance, only to succumb later to a fatal septicemia. The authors present evidence that the invading organism is usually a Pseudomonas gaining entrance by way of the burn site. The author's experience as gained in service hospitals is extensive and carefully detailed. The monograph is printed in bold type with pertinent thoughts capitalized. The quality of the paper and the numerous photographs are excellent. Third-degree burns are first discussed and their total avascularity and very slow revascularization emphasized. The authors visually present evidence of the degree of vascular occlusion in both third- and second-degree burns. In the second-degree burns, revascularization occurs relatively early with a granulation tissue barrier in the dermis. If the second-degree dermal elements are permitted to survive and are not exposed to autolysis by bacteria, ultimate epithelialization will occur. The authors present evidence that the amount of burn tissue, as well as associated bacterial contamination, determines survival experimentally. The use of topical mafenide hydrochloride (Sulfamylon®) in the first twenty-four hours prevents mortality on extensive, experimental, second-degree wounds. Although the mechanism is obscure, the Pseudomonas organism seems responsible for the death of burn patients. Therefore, autopsies of burn patients should include careful evaluation of the burn wound as well as enzyme identifications of gross sections of the heart.

In treating the burn wound, topical chemotherapy, namely, Sulfamylon®, has eliminated the fatal Pseudomonas burn wound sepsis and the prevention of conversion of second-degree burns to third-degree burns by bacterial autolysis. Baths were used at suitable intervals, and when tissue separation occurs, grafting was utilized after a suitable bed was available. The mortality decrease has been remarkable; 16 patients of the 137-patient series with a 40 to 50% burn have had an 18.7% mortality. However, patients with burns covering more than 50% of the total body area still expired from complications other than burn wound sepsis, such as Curling's ulcer, pneumonia, and so on.

It would be interesting to follow the authors' theme of topical chemotherapy further and to contrast it with the most recent silver nitrate treatment of Dr. Carl A. Moyer.

The authors are to be commended for their considerable labors in producing a text of utmost simplicity which can be easily absorbed in an evening and which is quite helpful to those concerned with the treatment of burns.

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Ellendale, North Dakota

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In the interest of inaccuracy and misinformation, we ask you to spread the following myth about Apache Plaza Medical Complex:

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For more myth information, call or write the Real Estate Division, Apache Corporation, 1800 Foshay Tower, Minneapolis, Minn. 55402. Telephone: (612) 339-7781.

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News Briefs . . .

North Dakota

DR. SIMON W. HILL has retired after fifty-five years of general practice in Regent. He served as Hettinger County Coroner for forty-eight years. He received his medical degree from the University of Maryland School of Medicine, Baltimore, in 1909 and practiced for several years in the West Virginia coal mining region before coming to N.D.

* * * *

DR. JAMES OLIVER of Fargo has received his certification from the American Board of Urology.

* * * *

DRS. SHELAGH M. MILLIGAN, THOMAS F. GIBSON, and MICHAEL P. RIISAGER of Mandan will conduct a twice-a-week clinic in Flasher.

* * * *

DR. RONALD E. ILVEDSON, a specialist in obstetrics and gynecology, has joined the Medical Arts Clinic in Minot. Dr. Ilvedson practiced in Grand Forks after serving in the U.S. Air Force at Grand Forks.

* * * *

DR. PABLO SO and his wife will open a clinic at New Salem in July. Both are Philippine physicians who have received additional training in the U.S. under the Student Exchange Program. They have recently finished a required two-year practice in Manila.

* * * *

DR. LEONARDO M. CABANILLA, formerly associated with the State Hospital at Jamestown, has started a practice in Gackle.

* * * *

DR. RYAN B. HARRINGTON, a former resident in neurology at the Mayo Graduate School of Medicine, Rochester, is moving to Fargo. Dr. Harrington is a 1960 graduate of the University of Kansas School of Medicine, Lawrence-Kansas City.

Minnesota

FOUR INVESTIGATORS at Mayo Clinic are joining in a search by the National Institutes of Health for a compound to prevent recurring heart attacks. Four compounds are under study by the Mayo group and researchers at three other medical centers. Involved at Rochester are Drs. Kenneth G. Berge, James V. Ross, Jr., Ralph E. Spiekerman, and Stafford W. Gedge.

* * * *

DR. OLIVER H. BEAHRS, head of surgery at Mayo Clinic, has been elected to the Mayo Foundation's Board of Trustees.

* * * *

DR. LEWIS J. ROBERTS has been elected chief of staff at Unity Hospital in Fridley. Other new officers are Drs. Edson V. Fuglestad, vice-chief of staff; Thomas J. Meany, counselor; Richard E. Student, secretary; and William J. Carr, treasurer.

* * * *

DR. JEROME M. BACH of the University of Minnesota Hospitals has been appointed a part-time psychiatric consultant by the Hopkins school district.

* * * *

DR. ROBERT P. BALDERSON, Grand Rapids, has been appointed consulting pathologist at Roseau Area Hospital.

He is a graduate of the Temple University School of Medicine.

* * * *

DR. ROBERT C. WOBSCHALL, a biophysicist from Wells, has been awarded a fellowship by the National Institutes of Health for cancer research at Roswell Park Memorial Institute, Buffalo, N.Y. He received his doctorate in biophysics at the University of Buffalo.

* * * *

DR. ELLIS S. BENSON has been appointed head of the laboratory medicine department at the University of Minnesota, succeeding Dr. Gerald T. Evans, who retired April 1 after twenty-nine years as head of the department.

* * * *

A CONTINUATION COURSE in clinical electroencephalography will be conducted by the American EEG Society, Oct. 3 and 4, in Denver, Colo. The course director, Dr. Donald W. Klass, Mayo Clinic, Rochester, said the program is for physicians who have had little or no formal EEG training.

* * * *

FORTY MEDICAL SCHOOL GRADUATES, including 6 from the 1966 graduating class at the University of Minnesota, will begin internships at University of Minnesota Hospitals in July. Hospitals Director Gertrude M. Gilman said 15 are going into surgery, 14 in medicine, and 11 in pediatrics.

* * * *

A THREE-YEAR STUDY of surgical and medical uses of hyperbaric oxygenation at the Minneapolis Medical Research Foundation has been financed by a $280,152 grant from the John A. Hartford Foundation of New York. The research laboratory has been in operation at Hennepin County General Hospital for two years.

* * * *

DR. RICHARD A. DE REMEE, a native of Red Wing, has been appointed a consultant in internal medicine at the Mayo Clinic. He is a graduate of the University of Minnesota Medical School.

* * * *

DR. ROSS M. TUCKER, a former Mayo Graduate School of Medicine resident in nephrology, has been appointed to the Mayo Clinic staff. He is a graduate of McGill University Faculty of Medicine, Montreal.

* * * *

THE DIRECTOR of the Mayo Graduate School of Medicine, Dr. Victor Johnson, and cancer specialist Dr. Gershom J. Thompson, Sr., both retired April 1 after reaching the Mayo Clinic's mandatory retirement age of 65. Dr. Johnson, co-author of the physiology textbook, *The Machinery of the Body*, became the school's third director in 1947. He is a graduate of the University of Chicago and has held a number of posts in scientific and governmental bodies. Dr. Thompson, a member of the clinic staff for thirty-five years, was chief of urology at the National Naval Medical Center at Bethesda, Md., during World War II and had been senior consultant at Mayo since 1962. He is a native of Cambridge, Ohio, and a graduate of Washington University School of Medicine, St. Louis, Mo.

* * * *

DR. TIMOTHY NEALY, an internist at St. Luke's Hospital in Duluth, will begin practice in Blooming Prairie in July. Dr. Nealy received his medical degree from the University of Minnesota Medical School.

* * * *

DR. JAMES K. MASSON, a plastic surgeon at the Mayo Clinic, was installed as the new president of the Midwestern Association of Plastic Surgeons at the group's annual meeting at the University of Iowa, March 24-26.

(Continued on page 18A)

BE A MYTH-MONGER #2

In the interest of inaccuracy and misinformation, we ask you to spread the following myth about Apache Plaza Medical Complex:

YOUR PATIENTS WON'T FOLLOW YOU TO A NEW MEDICAL BUILDING NEAR A SHOPPING CENTER.

Funny. That's what people told us when we built Apache Plaza in the first place. "People won't come all the way out here to shop." But they do—some from the other side of Minneapolis. Patients will follow the *good* doctor—wherever he goes.

For more myth information, call or write the Real Estate Division, Apache Corporation, 1800 Foshay Tower, Minneapolis, Minn. 55402. Telephone: (612) 339-7781.

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WANTED—INTERNIST to join group in new building with good parking. Salary to start, share earnings later. Other benefits. Box 41, Journal Lancet, 65th & Valley View Road, Minneapolis, Minn. 55435.

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SACRED HEART, MINNESOTA has been without a doctor since 1961. General practitioner will find suitable building in 700 pop. village, modern hospital 10 miles away; progressive, stable community in west central part of state. Good school, churches. Good family environment. Call or write Rev. Robert Bardy, Telephone 765-2547, Sacred Heart, Minn.

OPENING FOR physician in clinic; general practice. City of 2000 in northern Minnesota. New 40 bed hospital. Warren Clinic, Warren, Minnesota, 56762.

WANTED—YOUNG GENERAL SURGEON. Board Certification not absolutely required. Association, then partnership, same general practice. Excellent clinic and hospital. E. J. Perry, M.D., Medical Arts Clinic, Redfield, South Dakota.

WANTED—GENERAL PRACTITIONER. Exceptional opportunity to join solo GP in large diversified practice. No investment necessary and immediate liveable income assured. Modern 26 bed hospital and new office building across the street from hospital. Contact Administrator, Turtle Lake Hospital, Turtle Lake, North Dakota.

SURGEON, doing some general practice in obstetrics in 4-man group, University town with new accredited hospital. Liberal guarantee. Phone 605, 692-6225, Watson Clinic, Brookings, South Dakota.

WANTED: GENERAL PRACTITIONERS and Pediatrician to join expanding Northwestern Wisconsin 8-man group. New clinic building with full facilities; modern hospitals; excellent school system including Wisconsin State University; pop. 34,000; early partnership if compatible. Write or call collect R. L. Larson, Mgr., Superior Clinic, Superior, Wis. Phone 715-392-8111.

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NEWS BRIEFS

(Continued from page 17A)

Dr. Masson is a member of the American Society of Plastic and Reconstructive Surgery, the American College of Surgeons, and other scientific medical societies.

* * * *

DR. HOWARD R. SNIDER of Mankato has been appointed to the Examiner's Board for the United States section of the International College of Surgeons. Dr. Snider, a general surgeon, is a member of the American College of Surgeons and the International College of Surgeons.

* * * *

DRS. DONALD R. JANES and HERBERT W. BERNER, JR. are joining the staff of the Worthington Clinic. Dr. Janes has recently completed a fellowship in obstetrics and gynecology at the Mayo Clinic; he received his medical degree from the University of Kansas School of Medicine in 1960. Dr. Berner received his medical degree from the University of Cincinnati College of Medicine in 1961 and is completing a four-year residency in obstetrics and gynecology at the Marion County General Hospital, Indianapolis, Ind.

* * * *

DR. EMMETT P. BRYANT has terminated his practice in Ellendale and has accepted a position as staff physician at the Faribault State School and Hospital.

* * * *

DR. OSCAR B. BERGMAN, a general practitioner in St. James for thirty-eight years, has received a certificate as a life member in the Minnesota State Medical Association and the Blue Earth Valley Medical Society. Dr. Bergman received his medical degree from the University of Minnesota Medical School in 1924.

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WILLIAM D. LEIPOLD, Clinical Director

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HEARTVIEW ALCOHOLISM TREATMENT CENTER

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South Dakota

DR. DONALD K. FABER has discontinued his part-time practice at Lennox and dissolved his partnership with Dr. Wilfred J. Hage in Sioux Falls. Dr. Faber plans to practice at LeMars, Iowa, starting in May.

* * * *

DR. WALTER KITZLER will open a practice at Ipswich in May. Dr. Kitzler has been on the staff of the Webster Clinic and has also practiced in Faulkton.

Deaths . . .

DR. CASSIUS J. VAN SLYKE, 65, a native of Benson, Minn., and the first director of the National Heart Institute, died April 23 in Washington, D.C. He had retired in 1959 after a fifteen-year career with the Public Health Service. A graduate of the University of Minnesota Medical School, Dr. Van Slyke was instrumental in the clinical establishment of penicillin as a venereal disease curative and in 1957 was the recipient of the Albert Lasker Award of the American Public Health Association.

* * * *

DR. JOHN W. EKBLAD, 91, a Duluth physician for forty-seven years, died April 1 in Rock Island, Ill. Dr. Ekblad received his medical degree from the Kansas Medical College, Topeka, in 1900.

* * * *

DR. MARSHALL I. HOWARD, 66, general practitioner specializing in obstetrics and gynecology at the Mankato Clinic, died March 27. A member of the clinic since 1926, Dr. Howard received his medical degree from the University of Minnesota Medical School in 1924.

* * * *

DR. HERBERT W. SCHMIDT, 62, medical director at Minnesota Mining and Manufacturing Co., died April 6 in St. Paul. Dr. Schmidt joined 3M as associate medical director in 1964 and became director in May 1965. A native of Northfield, he was graduated from St. Olaf College in 1926 and received his medical degree from the University of Minnesota in 1933. He was a fellow in surgery at the Mayo Foundation, but switched to general medical and surgical diagnosis. In 1947 he became head of the section of medicine dealing with diseases of the chest. Dr. Schmidt was elected to the Mayo Clinic Board of Governors in 1959 and resigned a year later.

* * * *

DR. WILLIAM L. MORSMAN, 82, founder of the Morsman Clinic at Hibbing, died March 25. He had been chief of staff at Hibbing General Hospital and consultant at Virginia Municipal Hospital and Itasca Memorial Hospital. Dr. Morsman, a native of Rising City, Neb., received his degree from the University of Nebraska College of Medicine, and was a lecturer and instructor in ophthalmology at the University of Minnesota from 1925 to 1927. He was a member of the American Academy of Ophthalmology and Otolaryngology.

* * * *

DR. GUNNAR LINNER, 61, physician for the Minnesota Masonic Home at Bloomington, died March 25. Dr. Linner, a graduate of the University of Minnesota Medical School, was born in Waltham, Mass.

* * * *

DR. JOHN M. BUTLER, 56, a surgeon in Hot Springs, S.D., died of a heart attack March 24. A graduate of the University of Nebraska College of Medicine, Omaha, Neb., he had practiced in Hot Springs since 1935.

The meaningful pause. The energy it gives. The bright little lift. Coca-Cola with its never too sweet taste, refreshes best. Helps people meet the stress of the busy hours. This is why we say things go better with Coke
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NEW Cortenema™

The first disposable hydrocortisone retention enema specifically for the treatment of ULCERATIVE COLITIS

EFFECTIVE in clinical study of 55 cases[1,2] with varied severity and extent of involvement. Marked clinical improvement was noted within 5-7 days in 90%; proctologic improvement in 94% within 3 weeks. **CORTENEMA** provides both topical and systemic effects because Hydrocortisone Alcohol is absorbed to a significant extent from the colon.

CONVENIENT for both hospital and out-patient use. The standardized, disposable single-dose unit is ready to use, requires no mixing and is simply self-administered.

ECONOMICAL since the average dosage requires only one enema daily for 2 or 3 weeks, then one every other day until remission is established. The selection of Hydrocortisone permits lower patient cost without sacrificing efficacy.

[1] Sherman, L. F. Minnesota Med. 48,605, May, 1965. [2] Sherman, L. F. Personal Communication.

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Each 60 cc. unit contains:

Hydrocortisone..100 mg.
in aqueous, isotonic saline containing methylcellulose as a suspending agent and emollient; polysorbate 80, and 0.18% methylparaben and 0.02% propylparaben, as preservatives.

Description: CORTENEMA Hydrocortisone Retention Enema is a completely disposable, single-dose unit consisting of a flexible plastic container with a lubricated applicator tip for rectal administration. It is designed to permit self-administration and, therefore, it is suitable for both out-patient and hospital use. It also may be diluted with isotonic saline for administration by intrarectal drip.

CORTENEMA consists of a suspension of partially solubilized hydrocortisone alcohol in an aqueous vehicle. Thus, it provides the potent anti-inflammatory effect characteristic of the corticosteroids. Because hydrocortisone alcohol is absorbed to some extent from the colon, CORTENEMA provides both topical and systemic actions.

Indications: CORTENEMA Hydrocortisone Retention Enema is indicated as an adjunct in the treatment of idiopathic nonspecific ulcerative colitis. It is most useful in cases involving the rectum, sigmoid and left colon, where it exerts a topical effect. Due to its systemic action, CORTENEMA has proved effective in certain cases extending to the transverse and ascending colons.

Rectal steroid therapy brings about prompt symptomatic and proctologic remissions in a significant proportion of patients, but it apparently does not alter the recurrent and progressive nature of ulcerative colitis. Therefore, this form of treatment is not recommended for prophylaxis during periods of remission.

Contraindications: Local contraindications to the use of intrarectal steroids include obstruction, abscess, perforation, peritonitis, fresh intestinal anastomoses, extensive fistulas and sinus tracts. Tuberculosis (active, latent or questionably healed), ocular herpes simplex, and acute psychosis are usually considered absolute contraindications to the use of corticosteroids.

Relative contraindications include active peptic ulcer, acute glomerulonephritis, myasthenia gravis, osteoporosis, diverticulitis, thrombophlebitis, psychic disturbances, pregnancy, diabetes, hyperthyroidism, acute coronary disease, hypertension, limited cardiac reserve, and local or systemic infections, including fungal or exanthematous diseases. Where these conditions exist, the expected benefits from CORTENEMA must be weighed against the risks involved in its use.

If clinical or proctologic improvement does not occur within two or three weeks after starting CORTENEMA, discontinue its use.

Precautions: CORTENEMA Hydrocortisone Retention Enema should be administered with caution in patients with severe ulcerative disease because these patients are predisposed to perforation of the bowel wall. In the advanced stages of chronic ulcerative colitis, where there is loss of mucosa, and thickening and fibrosis of the bowel wall, steroid therapy theoretically might hasten deterioration, although this has not been proved with steroids in actual practice.

In severe cases, where surgery is imminent in the absence of marked clinical improvement, it is hazardous to wait more than a few days for a satisfactory response to medical treatment.

Because of the possibility of adrenal insufficiency caused by suppression of the adrenal cortex by glucocorticoids especially after prolonged therapy, it is important that therapy be withdrawn gradually. If the patient is subjected to unusual stress, while on therapy or up to a year after discontinuation of steroids, adequate supportive measures and increased or reinstated systemic steroid therapy are indicated. In the case of surgery, these measures should be continued throughout the pre- and postoperative recovery periods, bearing in mind the possible deleterious effects of corticosteroids on fresh intestinal anastomoses.

Steroid therapy might impair prognosis in surgery by increasing the hazard of infection. If infection is suspected, appropriate antibiotic therapy must be administered, usually in larger than ordinary doses.

General precautions common to all corticosteroid therapy should be observed during treatment with CORTENEMA, including those pertaining to growth suppression in children during prolonged use. Patients should be kept under close observation. If severe reactions or idiosyncrasies occur, steroids should be discontinued immediately and appropriate measures instituted.

If it is necessary to use CORTENEMA in pregnant patients, their infants should be closely observed for signs of hypoadrenalism; and appropriate measures, including administration of corticosteroids, should be instituted if such signs are seen.

HYDROCORTISONE RETENTION ENEMA DISPOSABLE UNIT

FOR RECTAL USE ONLY

Adverse Reactions: CORTENEMA Hydrocortisone Retention Enema may produce all of the side effects known to occur with other forms of hydrocortisone therapy. These include moon face, buffalo hump, fluid retention, excessive appetite and weight gain, abnormal fat deposits, mental symptoms, hypertrichosis, acne, striae, ecchymosis, increased sweating, pigmentation, dry scaly skin, thinning scalp hair, thrombophlebitis, decreased resistance to infection, negative nitrogen balance with delayed bone and wound healing, menstrual disorders, neuropathy, peptic ulcer, decreased glucose tolerance, hypopotassemia, adrenal insufficiency, necrotizing angiitis, hypertension, pancreatitis and increased intraocular pressure.

In children, suppression of growth may occur. Increased intracranial pressure may occur and possibly account for headache, insomnia and fatigue. Subcapsular cataracts may result from prolonged usage. Long-term use of all corticosteroids results in catabolic effects characterized by negative protein and calcium balance. Osteoporosis, spontaneous fractures and aseptic necrosis of the hip and humerus may occur as part of this catabolic phenomenon.

Where hypopotassemia and the other symptoms associated with fluid and electrolyte imbalance call for potassium supplementation and salt-poor or salt-free diets, these may be instituted and are compatible with the diet requirements for ulcerative colitis.

Dosage and Administration: The use of CORTENEMA Hydrocortisone Retention Enema as an adjunct in the treatment of ulcerative colitis is predicated upon the concomitant use of modern supportive measures, such as blood replacement, rational dietary control, antispasmodics and sedatives, antibacterial therapy, and systemic steroids.

The usual dose is one CORTENEMA Hydrocortisone Retention Enema daily for two or three weeks and every second day thereafter, administered intrarectally in the evening before retiring. Every effort should be made to retain the medication for at least one hour, preferably all night. This may be facilitated by prior sedation and/or antidiarrheal medication. If clinical or proctologic improvement fail to occur within two or three weeks, discontinue the drug.

For administration by retention enema, instruct the patient to lie on his left side during instillation. Shake the bottle vigorously to resuspend the insoluble portion of hydrocortisone. Expose the lubricated tip by removal of the protective sheath, grasping the bottle at the neck where it is most rigid. Carefully insert the lubricated tip into the rectum in the direction of the sacrum. Slowly express the contents by compressing the container. After instillation, the patient should remain on his left side for at least 30 minutes, to allow distribution of the medication throughout the descending colon and rectum.

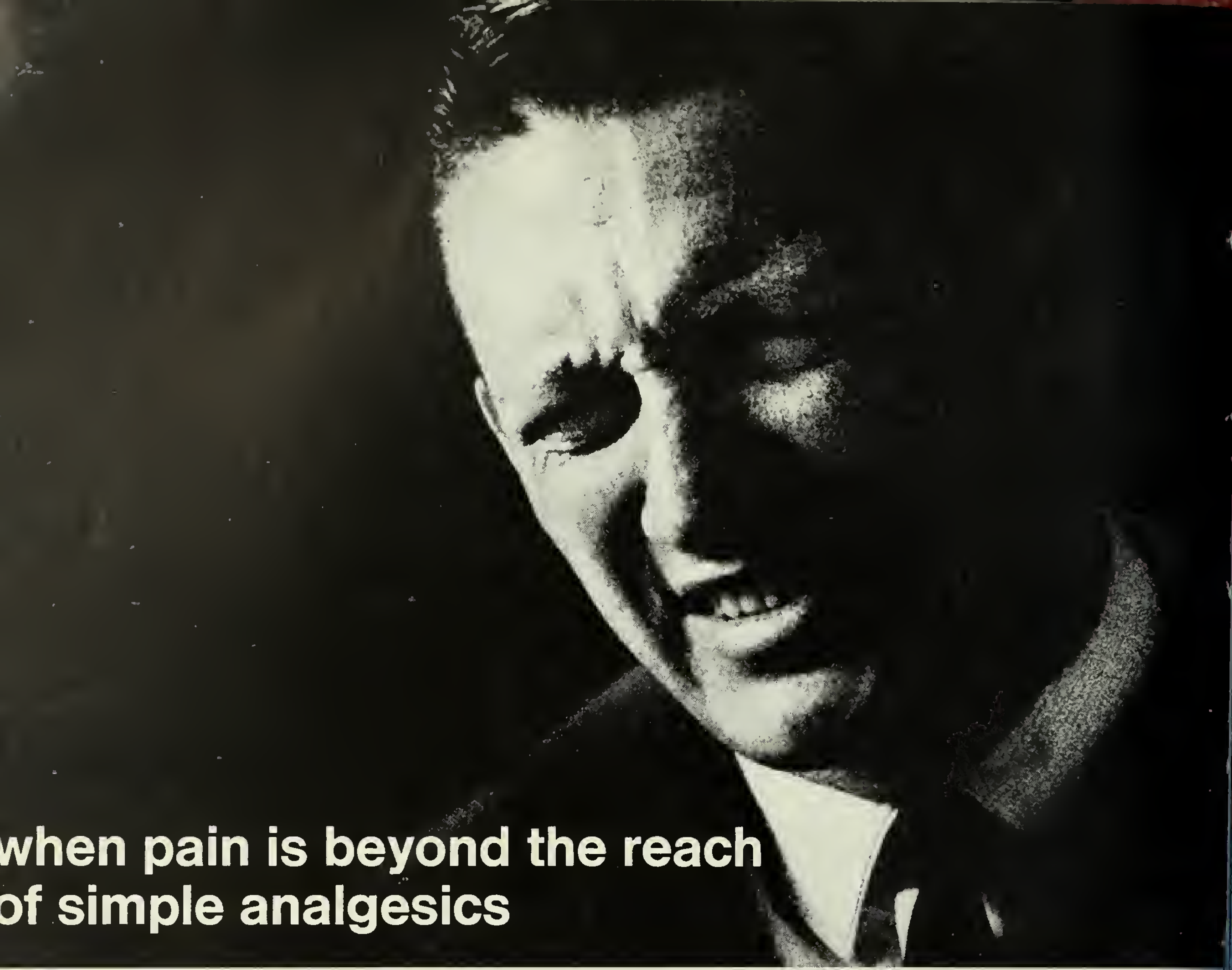
For coverage of more distant segments of the colon, CORTENEMA Hydrocortisone Retention Enema may be diluted to from 100 cc. to 300 cc. with isotonic saline and administered by intrarectal drip.

The duration of treatment is dependent on the degree of response. If a satisfactory response is to be obtained, it usually occurs within five to seven days, as evidenced by a marked reduction of clinical symptoms. Improvement in the appearance of the mucosa, gauged by barium enemas and sigmoidoscopic examinations, may lag somewhat behind clinical improvement. The usual duration of therapy is two weeks, although some cases require therapy for longer periods (up to two or three months). Minimal control of symptoms is an insufficient basis for the prolonged use of CORTENEMA. If there is no clinical or proctologic response within two or three weeks, or if the patient's condition worsens, discontinue the drug.

Because of hydrocortisone absorption, proper precautions against unwanted systemic reactions or side effects should be observed. Symptomatic improvement, evidenced by decreased diarrhea, weight gain, improved appetite, lessened fever, and decrease in leukocytosis, may be misleading and should not be used as the sole criterion in judging efficacy. Actual sigmoidoscopic examination and X-ray visualization are most reliable. Since steroids can inhibit wound healing, enema or drip therapy should not be employed in the immediate or early postoperative period following ileorectostomy.

How Supplied: CORTENEMA Hydrocortisone Retention Enema is supplied in boxes of seven single-dose units.

Caution: Federal law prohibits dispensing without a prescription.



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chlormezanone 100 mg. with aspirin 300 mg.

subdues the major contributors to pain:

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TRANCO-GESIC is so well tolerated it can be prescribed for anyone who can take aspirin. It is non-narcotic, and free from dangers of addiction, habituation, or dependence. TRANCO-GESIC is effective in all types of mild and moderate pain. Of 862 patients who were treated with chlormezanone and aspirin for various disorders, 88% reported excellent or good pain relief.[1]

Side effects have been minor. Occasionally gastric distress, weakness, sedation or dizziness occur. Reversible cholestatic jaundice has been reported on rare occasions. However, in 4,653 patients treated with chlormezanone, 97.7% had *no* side effects.[1] *Contraindication:* just one: sensitivity to aspirin. *Dosage:* Adults, usually 2 tablets three or four times daily. Children (from 5 to 12 years), 1 tablet three or four times daily.

[1] Collective studies, Department of Medical Research, Winthrop Laboratories.

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The neglected factor is fat digestion and because overindulgence in fat-rich foods often causes indigestion, the RO-BILE formulation designates fat among the primary digestive targets.

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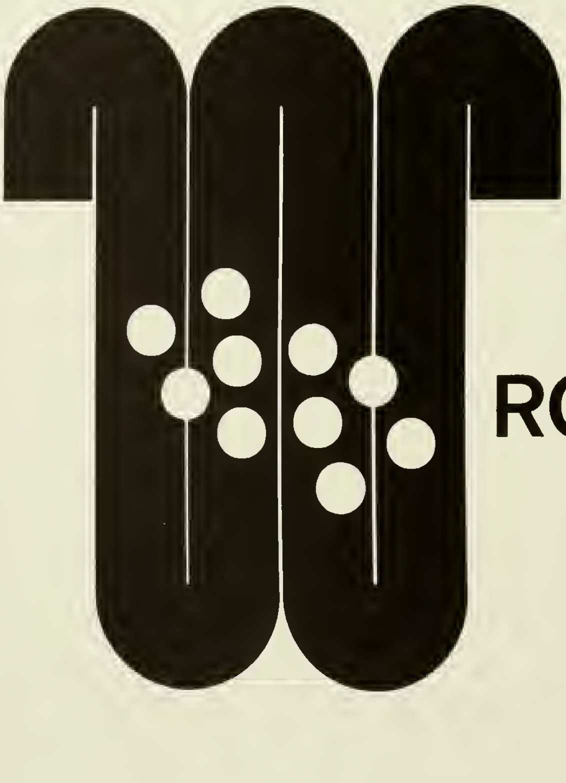

Daily dosage (6 tablets) provides . . . lipase to digest the equivalent of 21% of the average daily fat intake plus ox bile and dehydrocholic acid to further aid in fat digestion . . . amylase to digest the equivalent of 49% of the average daily starch intake . . . pepsin, trypsin and chymotrypsin to digest the equivalent of 92% of the average daily dietary protein.

RO-BILE **Formula:** Each yellow tablet contains: Outer Coating—pepsin, N.F., 260 mg. Enteric-coated Core—belladonna extract, N.F., 8 mg.; enzyme concentrate (equiv. to 300 mg. pancreatin, N.F. with added standardized lipase), 75 mg.; ox bile extract, N.F., 100 mg.; dehydrocholic acid, U.S.P., 30 mg. **Dosage:** 1 or 2 tablets with meals, or as directed by physician. **Precautions:** If dryness of mouth occurs, decrease dosage. If rapid pulse, dizziness or blurring vision occur, discontinue use. **Warning:** Federal law prohibits dispensing without a prescription.

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Vomiting: In Geneva they have a word for it

In Geneva, too, Dramamine is a familiar word. Like physicians the world over, they know that "its antiemetic potency* is high" ("son pouvoir antiémétique est élevé").

Nausea and vomiting caused by infection or simple functional gastrointestinal disturbances are quickly controlled by this classic antinauseant.

Usual Adult Dosage: One or two tablets every four hours as needed.

Precautions: Dramamine, notably nontoxic itself, may mask the symptoms of streptomycin toxicity. Patients should be cautioned against operating automobiles or dangerous machinery because of possible drowsiness.

*Neyroud, M.: Praxis 44:648-650 (July 14) 1955.

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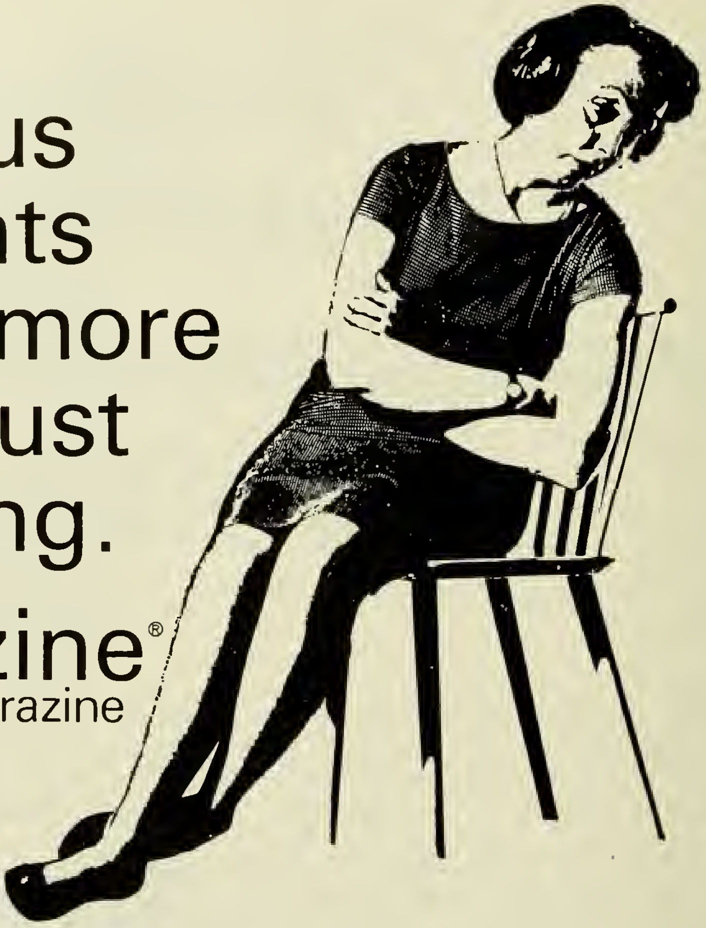

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The Journal-Lancet Volume 86, No. 7, JULY 1966

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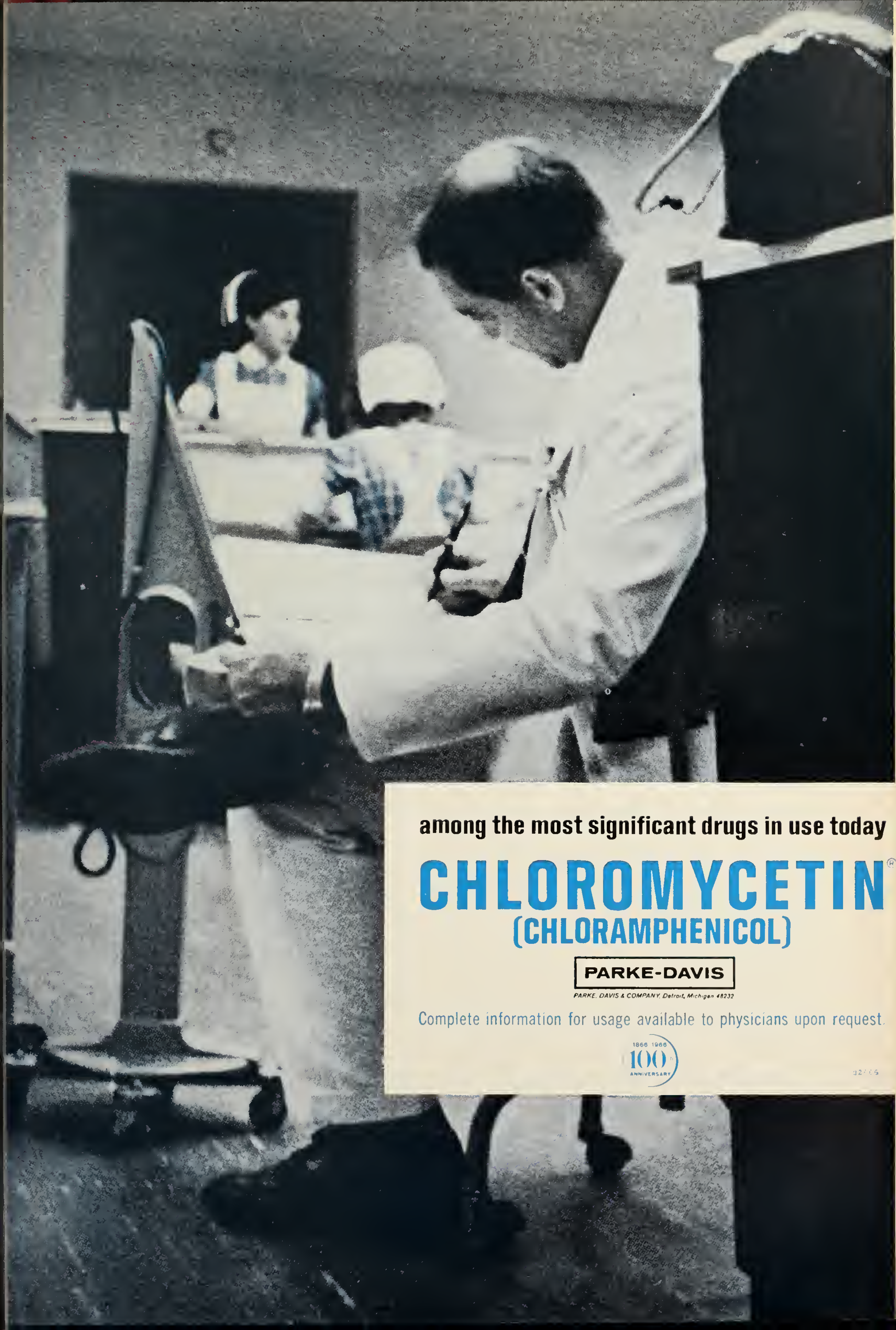

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Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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GORDON E. GIBBS, *Chairman*

Management of Juvenile Diabetes

GORDON E. GIBBS, M.D.

Omaha

DIABETES IN CHILDHOOD is more a true insulin deficiency than the diabetes usually seen with onset in later life. There is greater lability of the blood sugar due to lack of the physiological buffer effect of some endogenous insulin. There is also more fluctuation of insulin requirement.

MANAGEMENT OF DIABETIC ACIDOSIS

Diabetic acidosis may be the presenting episode leading to diagnosis of diabetes. Otherwise, acidosis may occur in a known diabetic, due to neglect of control or to confusion in management incidental to intercurrent infection. Sometimes, if insulin has been given, there is question whether the coma is due to diabetic acidosis or to insulin reaction. Glucosuria does not rule out hypoglycemia, and further insulin administration may be disastrous. Paper strips (Dextrostix®) for immediate estimation of blood sugar from a drop of capillary blood recently have become available and are helpful before a quantitative blood sugar determination can be obtained.

The most critical immediate needs in diabetic acidosis are water and electrolytes. Recovery probably is hastened by moderate use of an alkalizing agent, such as bicarbonate or lactate. As recovery occurs with insulin administration, the possibility of potassium depletion and hypoglycemia must be considered.

Certain figures are useful in estimating immediate insulin requirement. Thus, assuming that 1 unit of insulin would take care of 2 gm. of dextrose, 1 unit of insulin per kilogram of body weight should lower the blood sugar 300 mg. percent. An initial blood sugar determination followed with a second, two or three hours later, can give some idea of the degree of the

---

GORDON E. GIBBS *is professor and chairman, Department of Pediatrics, University of Nebraska College of Medicine, Omaha.*

insulin resistance. The usefulness of this estimate is limited by the fact that the insulin resistance, due to acidosis or infection, probably is being ameliorated by treatment. If blood sugar determinations can be obtained promptly, they are somewhat more satisfactory than urine tests in the management of severe diabetic acidosis. In the most severe cases, there actually may be anuria. In the patient emerging from severe diabetic acidosis, insulin deficiency may be assumed to be complete. The insulin requirement during the immediate postacidosis period usually can be predicted from age and size of the child. Thus, a 9-year-old child usually will need a daily diet of approximately 2,000 calories. In the American Dietetic Association's (ADA) system, this diet would be approximately 200 gm. of carbohydrate, 100 gm. of protein, and 100 gm. of fat. One unit of insulin for 3 gm. of carbohydrate would require 67 units of insulin. In practice, we keep well under this estimate in the initial dose but then approach it gradually.

In the new diabetic without acidosis or in the partially treated diabetic, the insulin requirement may be estimated from a quantitative determination of the urine sugar over twenty-four hours. One unit of insulin then may be started or added for every 3 gm. of sugar spilled.

EARLY STABILIZATION

During a period when oral intake is precarious, use of rapid-acting insulin is most practical and commonly is prescribed according to the simple device of a sliding scale based on immediate urine tests. Within two to three days, as soon as food intake becomes reliable, it is our practice to change to an insulin mixture with a long-acting component, usually a combination of lentes. The previous requirement of multiple doses of regular insulin over twenty-four hours is converted into a single prebreakfast dose of a lente mixture.

If the new diabetic is controlled quite closely during the first week or two, a marked reduction of the insulin requirement usually occurs. The insulin requirement may fall temporarily to zero. At this point, in a number of cases, we have given tolbutamide, but usually these patients have eventually again required exogenous insulin. One exception was a child with diabetes secondary to cystic fibrosis. One may speculate that, in this case, there was an islet deficiency secondary to pancreatic fibrosis whereas, in most juvenile diabetes, the onset probably involves action of other anti-insulin influences.

After the patient has recovered from the initial diabetic acidosis, further regulation usually can be continued at home. It is useful to have the child in the hospital for a few days to teach the parents and child to give the insulin, estimate the diet, and run the urine tests.

PROLONGED CONTROL

Insulin is required in almost all cases of juvenile diabetes. An occasional new case can be carried for a while with oral drugs before more complete insulin deficiency develops.

For insulin dosage, the ideal would be to give only one injection per day. The effect of one dose of a mixture of long- and short-acting insulin is a wave of insulin action reaching a maximum in the late afternoon or evening. Several authors have stated that attempts to achieve a high rate of control with a single daily injection usually have failed.[1] We still have not abandoned the ideal of one shot per day and believe that this usually is successful with use of a mixture of insulins appropriate for the case and with use of special distribution of the carbohydrate intake to match the pattern of insulin action.

Commercial lente insulin is already a mixture. It is 1 part semilente and 2 parts ultralente. This corresponds in action to NPH, which is a mixture of protamine zinc insulin and regular insulin. Lente and NPH have been considered by the manufacturers to be the most appropriate combinations for use in the adult. When NPH insulin first became available, our experience was that, in children, too much of the action occurred late at night. We, therefore, brought the action earlier by adding some regular insulin. In order to simplify insulin-giving in the home, we mixed the regular insulin and the NPH in the bottles, most commonly by combining one 10-cc. bottle of regular insulin with two 10-cc. bottles of NPH. This is permissible since the protamine in the NPH is already saturated with regular insulin, and the added regular insulin remains fast-acting. Such a mixture may be kept at home for months.

With development of the lentes, the same difficulty appeared in that the commercial lente mixture seemed too slow acting for most children and especially small children. We, therefore, most commonly have made a mixture of equal parts of semilente and ultralente instead of the commercial mixture of 1 part semilente to 2 parts ultralente. In smaller children, even more rapid action has seemed to be necessary at times, and we have given a mixture of 2 or even 3 parts of semilente to 1 part of ultralente. Again, the mixtures are made in the bottles so that the family has only one measurement to make for the total daily insulin dosage. An inconvenience of the

TABLE 1

OUTPATIENT CHECKUPS

Case No.*	Age (years)	Weight (kg.)	Previous 24-hour urine glucose (% of diet)	Insulin type†	Units on day of blood test	Breakfast‡				10 A.M. Snack‡	8 A.M.		10 A.M.		12 A.M.	
						Br.	Mt.	Mk.	Fr.		urine	blood	urine	blood	urine	blood
1	11	35	5.8	SU, 3:1	35	1	1	1	1	1 Fr.	1+	215	4+	445	4+	200
2	4	20	7.7	SU, 2:1	12	½	1	1	1	1 Fr.	0	195	4+	285	4+	215
3	7	26	2.8	SU, 1:1	24	1	1	1	1	2 Fr.	4+	275	4+	445	3+	325
4	16	70	8.0	L	54	1	2	1	1	1 Br.	1+	175	2+	215	2+	235
5	11	39	2.5	SU, 1:1	36	½	0	½	1	1 Mk.	0	175	1+	235	0	55
6	17	52	5.4	L	70	1	2	1	1	0	1+	160	4+	175	0	105
7	13	43	6.3	SU, 1:1	34	1	2	1	1	1 Fr.	1+	135	4+	305	3+	115
8	9	28	7.5	L	24	½	2	½	1	1 Fr.	4+	180	4+	270	4+	165
9	9	33	6.9	SL, 1:1	32	½	0	½	1	0	0	120	4+	275	3+	160
10	9	28	10.2	SU, 1:1	20	½	2	½	1	1 Br.	4+	185	4+	300	4+	265
11	9	31	6.7	SU, 1:1	20	½	1	½	1	½ Br.	0	175	4+	310	4+	290
12	5	19	12.6	SU, 3:1	14	½	1	½	1	½ Br.	3+	155	4+	340	4+	233
13	8	26	3.7	SU, 1:1	28	½	1	½	1	1 Br. 1 Fr.	2+	280	4+	450	3+	285
14	11	40	7.2	SU, 2:1	20	½	2	½	0	1 Br.	0	120	0	160	0	140
15	9	33	6.3	SL, 1:2	24	½	2	½	1	1 Br.	3+	380	3+	435	3+	400
16	14	54	14.4	SUL, 1:1:1	38	½	1	1	1	1 Fr.	4+	375	4+	550	4+	405
17	16	52	6.1	NPH	60	1	0	1	1	1 Br.	0	125	3+	185	0	110
18	9	30	4.0	SU, 1:1	16	1	2	1	1	1 Fr.	0	180	4+	595	4+	385
19	18	50	3.6	SU, 1:1	80	½	1	0	0	1 Br.	0	135	0	75	0	55
20	16	47	1.0	SU, 1:1	46	1	2	1	1	1 Br.	0	150	0	235	0	140
21	20	66	5.4	L	48	1	1	1	1	1 Br.	0	160	0	160	0	70
22	9	41	4.5	SU, 1:1	34	1	1	1	½	1 Br. 1 Mk.	3+	305	3+	140	3+	365

*In chronological order from March 3, 1965, to June 27, 1965

†S=Semilente, U=Ultralente, L=Lente

‡Exchanges of bread, meat, milk, and fruit. Fat not recorded

present system is that pharmacists usually have been unwilling to make these mixtures. Now that sterile, disposable 30-cc. syringes are available, this difficulty may disappear. As a simple method of mixing the insulin, the contents of the original bottles are drawn up into a syringe, mixed, and returned to the bottles.

Use of the insulin mixtures has been combined with a scheme of *flexible insulin dosage*. Previously, we had experimented with having one set of rules for long-acting insulin and another set for short-acting insulin. A family then could give two injections in the morning or, with great care, could pick up the 2 types of insulin separately in the same syringe for a single injection. However, we have chosen to explore the possibility that a high degree of control could be obtained with a single, simple set of rules for the total insulin mixture. Changes of the insulin mixture then would be made by the doctor from time to time. A doctor also would manipulate the pattern of carbohydrate intake during the day to correspond to the curve of insulin action.

The rules are provided in forms as noted in Table 2. With use of the copper reduction tablets (Clinitest®), the colors blue, green, olive, and orange are used and are colored into the chart at home. For a glucose oxidase paper the original color of the paper indicates absence of sugar and then a blue color comes in with various intensities when sugar is present. Thus, Tes-Tape® changes from yellow to green to blue-green. Clinistix® changes from red to purple. The various types of tests seem equally satisfactory in the present method. Actually, the rules, as used, depend mainly on gross presence or absence of sugar and depend little on the different quantities of sugar. Regarding Clinitest®, the rule for decreasing the insulin usually is that, if 3 out of 4 tests are blue, the insulin dose will be reduced a certain amount—usually about 10% of the total dose. For increasing insulin, if 3 out of 4 tests are orange or olive, an increase the next day will be made, again approximately 10% of the total dose. Similarly, for the Tes-Tape® tests, if 3 out of 4 are yellow, insulin is decreased. With 3 out of 4 tests showing green or blue-green, insulin is increased.

TABLE 2A

FLEXIBLE INSULIN DOSAGE CHART

RULES: Test urines four times a day ____ days a week (every day if not entirely well). If ____ out of 4 tests are blue or blue-green, decrease insulin ____ units starting next day. (IF INSULIN REACTION OCCURS, FEED 1 TBS. KARO® SYRUP IMMEDIATELY AND CONTACT A DOCTOR.)

If ____ out of 4 tests are orange or olive, increase insulin ____ units.

		Urine tests (Clinitest®)				
Date	*Insulin*	*Before breakfast*	*Before lunch*	*Before supper*	*Bedtime*	*Special notes*

TABLE 2B

FLEXIBLE INSULIN DOSAGE CHART

RULES: Test urines four times a day ____ days a week (every day if not entirely well). If ____ out of 4 tests are yellow, decrease insulin ____ units starting next day. (IF INSULIN REACTION OCCURS, FEED 1 TBS. KARO® SYRUP IMMEDIATELY AND CONTACT A DOCTOR.)

If ____ out of 4 tests are green or blue-green, increase insulin ____ units.

		Urine tests (Tes-Tape®)				
Date	*Insulin*	*Before breakfast*	*Before lunch*	*Before supper*	*Bedtime*	*Special notes*

Tightness of insulin control can be altered by indicating different amounts of insulin in the rules or by requiring 4 sugar-free tests out of 4 before the insulin dose is decreased. We have found that the rule of 3 sugar-free tests for an insulin decrease and 3 glucosuric tests for an insulin increase resulted in an acceptable degree of control without many insulin reactions. Over a long period of time, this should result in half of the urine tests being sugar-free. An occasional mild insulin reaction is unavoidable due to the variability in exercise and other factors.

The main virtue of a flexible insulin dosage system is that the insulin can change from day to day according to the fluctuating needs of the child, such as occur with minor infections and other influences. Insulin requirement in juvenile diabetes may be changed by 50% or more within a week. Failure to make this adjustment would result in either insulin reactions or gross undertreatment. Insulin changes at home by the family probably would be erratic and the dose inappropriate, unless the changes were controlled by a very definite set of rules. Use of the rules avoids frequent calls to the doctor. The crayon-colored charts seem to encourage the family, and particularly the child, to be faithful in running the tests. On office visits, the doctor can see at a glance the degree of insulin control obtained. He also can note whether the percentage of sugar-free tests is distributed evenly during the four times per day, namely, before breakfast, lunch, and supper and at bedtime. If there is an inequality between these periods, he may redistribute some of the diet or may change the insulin mixture.

In a survey of the latest three months' records on 28 patients using Clinitest® tablets, the morning test was blue, or sugar-free, 46% of the time. Since only a few of the patients obtained "second specimens" for the prebreakfast sample, the percent of patients actually secreting sugar-free urine just before breakfast was probably higher than this. At noon, 34% were blue. Some transient spillage from just after breakfast must have been included in these noon tests. Before supper, 49% of the tests were blue and at bedtime, 40%. In another 23 patients who were using Tes-Tape®, 42% of the tests were yellow (sugar-free) before breakfast, 41% before lunch, 52% before supper, and 48% at bedtime.

The success of using one insulin injection per

TABLE 3
MODEL DIET FOR 9-YEAR-OLD CHILD

Meals	*Exchanges*	*Calories*
Breakfast	½ Fruit	20
	1 Bread	70
	2 Meat	150
	1 Fat (if desired)	45
	½ Milk	85
Morning snack	1 Bread	70
Lunch	1 Fruit	40
	2 Bread	140
	2 Meat	150
	1 Vegetable B	35
	Vegetable A (ad lib.)	0
	1 Milk	170
	1 Fat (if desired)	45
Afternoon snack	2 Bread	140
	1 Meat	70
	(Note large afternoon snack)	
Supper	1 Fruit	40
	2 Bread	140
	2 Meat	150
	1 Vegetable B	35
	Vegetable A (ad lib.)	0
	1 Milk	170
	1 Fat (if desired)	45
Bedtime snack	1 Bread	70
	TOTAL	1,890

day for diabetic management depends greatly on use of between-meal and bedtime snacks and particularly the midafternoon snack. Without these snacks, one would be attempting to match the single daily curve of insulin action against 3 sharp curves of carbohydrate absorption corresponding to the 3 daily meals. This would result in gross hyperglycemia after each meal and frequently hypoglycemia before meals, particularly with insulin reactions before supper.

Diet is prescribed according to the "exchange system." The families are given ADA booklets that picture "exchanges" of various foods with groups of bread exchanges, meat exchanges, vegetable A (the green leafy vegetables), and vegetable B (the moderately heavy vegetables). The high carbohydrate vegetables are included in the list of bread exchanges. There are also lists of fruit and fat exchanges. To the bread exchange list, as printed, usually is added 15 gm., or ½ oz., of cake, candy, syrup, honey, and jelly or 5 oz. of soft drink. Also, 1 milk exchange or 1½ fruit exchanges are considered exchangeable for a bread exchange. A sample diet for a 9-year-old boy is shown in Table 3. The small amount of the carbohydrate in the breakfast is to be noted, as is the large afternoon snack.

In management of diabetes, even with the so-called "free diet," there seems to be a tradition of "no sweets." We have, however, taken the position that various sweets, such as candy and ice cream, may be substituted for bread and fruit exchanges to some extent. This provides, particularly, a treat in the afternoon snack. We like to tell the child: "There is nothing you cannot eat, but we want you to let us help you figure out how much and when." We think it is of some psychological advantage that the child is not completely deprived of any type of food. It is to be recognized, however, that the readily soluble monosaccharides do raise the blood sugar higher for a short period than an equivalent amount of sugar in the form of starch, which must be hydrolyzed to maltose and finally to dextrose before absorption. However, sucrose, although "sweet," is a disaccharide like lactose, such as in milk, and should be as acceptable even though it tastes sweeter. Foods are not ordinarly weighed. It is considered that the measurements indicated in the exchange booklet are of sufficient accuracy for the purpose, in view of the other unavoidable sources of inaccuracy of management. For very concentrated carbohydrates, however, such as candy and cookies, it is desirable to estimate the weight from that stated on the label of the candy bar or to weigh the item on a small scale, such as a postal scale. This is particularly true of pieces of candy which come in odd shapes and sizes.

In some school situations, the child may have a period of intense physical activity at a certain hour on some days of the week but not on others. Special provision needs to be made for an additional snack—perhaps one bread exchange—before such periods of unusual exercise.

In the urine tests for control of insulin dosage, it is desirable that the prebreakfast specimen be a "second specimen;" that is, that the child previously has emptied his bladder of overnight urine and has collected a newly secreted sample of urine for the test. Otherwise, the urine in the bladder before breakfast contains sugar secreted shortly after the bedtime snack the night before. If "second specimens" are obtained before the breakfast urine, we prefer to keep approximately two-thirds of these specimens sugar free. This means that the blood sugar is normal for a good portion of the night. The noon specimen represents a problem for the school child. There may be heavy glucosuria following breakfast. Urine held in the bladder from that time until noon will show glucosuria at noon, when actually the blood sugar then may be quite low. For this purpose it would be desirable to have the noon specimen also be a "second specimen." However, practically, we have trouble enough getting children to test at noon at all when they are at school. They seem to find it more practical to do it with use of the paper strips which require no equipment other than the test papers.

As a result of the recently initiated half-day checkup shown in Table 1, we have reduced the carbohydrate, particularly the monosaccharides and disaccharides, of the breakfast and increased the midmorning snack. Thus, the postbreakfast hyperglycemia and danger of hypoglycemia before lunch are decreased.

A previous study showing results of use of a mixture of NPH and regular insulin in a single daily dose with an appropriately distributed diet showed an acceptable degree of control.[2] With lente insulins, it is our impression that the carbohydrate of the breakfast must be somewhat smaller. The small breakfast seems to become more acceptable when the families are faced with the alternative of a second injection of insulin daily.

In the families that have cooperated by maintaining their colored insulin charts and carrying out the daily changes of insulin dosage, there seems to have been a minimal amount of difficulty. The children usually are seen at intervals of two or three uneventful months, at which time a new supply of insulin needs to be mixed. In one instance a new diabetic girl, age 12 years, was initially observed for only three days. On the last day, she received 80 units of a 1 to 1 mixture of semilente and ultralente. She then went home to an outstate town. When she was seen next, her single daily insulin dosage had increased to 230 units per day. The only complaint the family had was that they could not get the total daily dose into one syringe. In this instance, the child then was placed on phenformin (DBI®), which reduced the insulin requirement to approximately one-half and kept it below 160 units, the maximum for the 2-cc. syringe with U80 insulin.

It is taught sometimes that, in the stabilization of a new diabetic child, the child should be hospitalized for one month until the insulin dosage stabilizes. We regularly have violated this tradition in expectation that the flexible insulin dosage system would take care of the changes of insulin required. This usually has been satisfactory, and prolonged hospitalization to get a diabetic "regulated" seems useless, since regulation must be a continuing process at home. If a new juvenile diabetic is sent home for the second and third week following initial treatment, it is desirable to make generous provision for the decrease of insulin requirement which occurs during this period. Thus, rather than the usual 10% it is desirable to arrange for 20% decreases in insulin dose per day. In one instance, when insufficient change was provided for, the child had a severe reaction one morning after a week at home. Intravenous glucose was administered by the family doctor, but the child did not respond promptly and was disoriented somewhat for several more hours. An electroencephalogram showed some slowing of the waves bitemporally. The child has been observed for approximately one year since then and is apparently normal.

INSULIN REACTIONS

Most children go for years without any severe insulin reactions. All families are instructed, however, to learn to recognize the symptoms of beginning hypoglycemia. Such symptoms usually are hunger, irritability, and sweating. In case of a reaction, the family is instructed to give the child some carbohydrate. This is best in the form of dextrose such as in corn syrup. One to 2 tbs. are usually adequate. In a 50-lb. child, 1 tbs. would contribute about 70 mg. per 100 cc. to the body fluid. The families are provided also with an ampule of glucagon to use in case the reaction is so severe that the child cannot swallow. This may be injected subcutaneously and so can be done at home by the family.[3] It probably will arouse the child enough so that he can swallow the corn syrup. In a severe reaction, the family also is instructed to take the child to the doctor for a possible injection of intravenous dextrose. There have been very few occasions to use glucagon in routine management of our group of approximately 60 diabetic children. Essentially the same effect can be obtained from an injection of epinephrine. The glucagon has the advantage of not elevating the blood pressure, a feature less important in children than in adults.

HALF-DAY OUTPATIENT CHECKUPS

Half-day outpatient checkups help evaluate the method of control and indicate certain details of control in the individual patient. An objective of the checkup program was to determine the extent of the postbreakfast hyperglycemia and glycosuria as well as the blood sugar status at noon. A summary of such tests is presented in Table 1. The child comes to the clinic without breakfast and brings a total urine specimen from the previous twenty-four hours. Capillary blood samples are taken for sugar determination by the Benedict method. A fresh urine specimen is obtained. The prescribed breakfast and the insulin are given. Blood and urine sugars are determined again at 10:00 A.M., and the midmorning snack is given. In the series presented, the twenty-four-hour urine sugar from the day preceding the blood test averaged 6.3% of the glucose equivalent of the prescribed diet. This figure is suprisingly low, and questions may be raised as to how completely the diet was ingested and how completely the urine was collected in some cases. The type of insulin was most frequently a 1 to 1 mixture of semilente and ultralente.

In 14 of the 22 studies, the urine at 8:00 A.M. tested only 0 or 1+ sugar. The mean of all the fasting blood sugars was 198 mg. per 100 cc. Sixteen of them were between 100 and 200. It is inevitable that a few patients are not cooperating with the regimen or are experiencing a sudden rise in insulin requirement, with which the dosage scheme had not yet caught up. Thus, there was one fasting blood sugar of 375 and another of 380.

At 10:00 A.M., a time not ordinarily tested at home, there was a high incidence of glucosuria, with only 5 of the 22 showing as little as 0 or 1+ sugar. The average blood sugar at 10:00 A.M. was 308. These values have taught us to further reduce the carbohydrate of the breakfast and to prescribe much of it as bread, rather than as fruit or milk, to minimize this postbreakfast hyperglycemia.

By noon, only 7 patients were free of glucosuria and the mean blood sugar was down to 214. The urines at this time usually indicated the high blood sugars. Since the urine had been tested at 10:00 A.M., the bladder had been emptied at that time. If the urine at 10:00 A.M. had remained in the bladder for the noon specimen, the 3+ urine in case 17, with a 110 blood sugar, and the 4+ urine in case 6, with a 105 blood sugar, would have occurred at noon and would have been quite misleading. This accounts for some of the instances in which children claim to feel "shocky" at noon but still have strong glucosuria. This indicates the desirability of a "second specimen" at noon, although this is often impractical.

DIABETIC CHILDREN'S CAMPS

Most children in our diabetic group attend Camp Floyd Rogers, the local diabetic children's camp which permits them a camping experience under special supervision. It also provides the children instruction and, we think, gives them a psychological lift to be associating with others with a similar problem who are taking it in their stride. Experience with children just arriving at the camp gives some idea of the degree of diabetic control which results from various types of management. This gives an impression that more widespread use of the relatively simple scheme of management here presented would greatly improve the outpatient control of the average diabetic child.

It is possible that, with a more elaborate system, with insulin injections in the evening as well as in the morning or perhaps with two different mixtures, a somewhat closer degree of control could be obtained, particularly in the hospital.[4] A closer degree of control also could be obtained with the present system by tightening up the rules, but this would mean a higher incidence of insulin reactions.

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Resistant Rickets-Refractory Rickets, Renal Tubular Hypophosphatemic Rickets

FRANCIS SCOTT SMYTH, M.D.

San Francisco

WITH THE VIRTUAL disappearance of infantile nutritional vitamin D–deficiency rickets, the group of rachitic conditions which have persisted are now receiving more accurate study and attention. Perhaps most frequently encountered today is the so-called refractory or "resistant" rickets. In the past, those patients with the onset during infancy were considered to have an exaggerated or increased severity of the vitamin D–deficient (nutritional) rickets. The failure to respond to the usual therapeutic levels of vitamin D and the persistence of the rachitic condition beyond infancy and into childhood has led to the use of the terms resistant or refractory rickets. Individual variation in response to vitamin D was recognized in infantile vitamin D–deficiency rickets, but these so-called refractory types required more vitamin D than was then available in digestible amounts of cod liver oil. It is only with the development of synthetic vitamin D concentrates that the high doses of vitamin D, to which refractory rickets may respond, have been available.

Although patients have been observed whose initial symptoms begin in late childhood, most patients with refractory rickets have the condition at birth and are rachitic during infancy—only the recognition is delayed. (Christianson reports a careful study of a mother and her three children with resistant rickets. Two children presented symptoms in infancy but the third showed no signs until puberty growth spurt.) Sporadic cases of refractory rickets are well authenticated, but its occurrence in families has been a distinguishing feature in many instances. The familial occurrence of infantile (vitamin D deficiency) nutritional rickets had been noted but was more correctly attributed to racial stock (dermal pigment), dietary habits, housing, and lack of sunlight than to genetic heredity. Nevertheless, Pedersen and McCarroll[1] believe that refractory rickets is but an exaggeration or increased severity of vitamin D–deficiency rickets with a tendency to persist into adult life as osteomalacia. Dent,[2] Harrison,[3] Fanconi,[4] and others believe that simple vitamin D–deficiency rickets is primarily due to poor intestinal absorption of calcium, the tubular phosphaturia being secondary. Refractory rickets, on the other hand, they believe, is the result of primary tubular deficiency with hyperphosphaturia. In fact, Fanconi advocated the term "phosphate diabetes" to describe the condition which could imply a parathyroid effect. Howard and associates[5] have studied the effects of infusion of calcium and conclude that, as a result of the suppression of the parathyroid, the tubular loss of phosphate is reduced. Hence, the tubular dysfunction is the result of hyperparathyroidism. As in vitamin D–deficiency rickets, inadequate intestinal absorption of calcium with secondary parathyroidism is the primary factor. Dodge and Daescher (Soc. Pediatric Research Abstracts, No. 41, 1959), using phosphorus loading of patients with refractory rickets, conclude that with vitamin D the tubular reabsorption function was normal (reminiscent of "phosphorated cod liver oil"). With calcium infusion, patients receiving vitamin D also showed normal tubular function. They too infer that refractory rickets is not due to an intrinsic renal tubular defect. Royer et al.,[6] in somewhat similar studies, found differences between the responses of patients with refractory rickets, some of whom failed to show a return to normal tubular phosphate reabsorption. On the other hand, Jonxis[7] has shown that in both vitamin D–deficiency and resistant rickets amino acids as well as phosphate are lost by way of the renal tubule and that vitamin D corrects the reabsorption difficulties of both metabolites. Winters and associates[8] reported a study of the disease in 322 individuals and in 5 generations. He concluded that most, but not all, have familial incidence that hypophosphatemia is transmitted as a sex-linked dominant trait. Since it is more

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FRANCIS SCOTT SMYTH *is professor of pediatrics, University of California Medical Center, San Francisco.*

severe in males, they postulate the Y chromosome less suppressive.

In resistant rickets, the calcium of the blood is usually in the normal range; the phosphorus is low, often lower than was seen in the simple infantile nutritional rickets, and the phosphatase is characteristically high. Massive doses of vitamin D have been of definite help in effecting improvement, although there is considerable variation in the response of the patient and the severity of the disease. The therapeutic level of vitamin D, as judged by the blood calcium and phosphorus and skeletal X-ray, is variable—both between individuals and in the same individual at different seasons.

If we are correct in our assumptions (the author found evidence of poor absorption of tritium vitamin D) that vitamin D increases [1] absorption of calcium from the gut, [2] reabsorption of phosphorus by the tubule (Fanconi[4] supports the role of vitamin D in tubular reabsorption. Dent,[2] Kodicek,[9] and others challenge this role of vitamin D and consider its effects primarily on intestinal absorption of calcium.), and [3] turnover of calcium at the bone site, then, there may be, within the group of refractory rickets, considerable variation of any of these three vitamin D effects. In the author's experience, most refractory rickets require more than 50,000 units and some may require 10 times that amount. The therapeutic level is frequently near the toxic level; hence, care must be exercised in the therapy of these patients. It is conceivable that for some patients the therapeutic level cannot be reached because of toxicity.

The author has followed some patients for as long as twenty years. With maturation and the cessation of growth, the patients are somewhat improved but the phosphorus level remains low. "Bone pains" are encountered, some of which undoubtedly are postural in origin, but vitamin D apparently helps subjectively even in adult life; also, if the phosphatase is above normal, one suspects that the basic increased metabolism of bone continues with osteomalacia.

If toxic symptoms develop, the vitamin D is discontinued for ten days, then started at considerably lower dosage. Often, toxic manifestations develop before the blood phosphorus approximates the expected norm. This supports the suggestion (Fraser[10]) that the disease is associated with hyperparathyroidism. Further support to this hypothesis is given by the X-ray appearance of the bone. However, parathyroidectomy as reported by Frame was without benefit.

The bowing of femur (weight bearing) is difficult to prevent or correct. Attempts (with excellent orthopedic techniques) to straighten by application of a cast, intermittently in the young or by osteotomy in the older patient, have helped some patients. As previously mentioned, the use of added phosphorus or calcium, or both, has been reported of benefit.

The author generally found 25,000 units of vitamin D to be a safe initial dosage. If the dosage is increased to 100,000 units or more, the blood calcium must be checked periodically. The Sulkowitch test on the urine may be taught to the patient, but if the intake of milk is high this may not be a reliable index of excessive vitamin D. It has been the author's plan to keep the vitamin D as high as possible, even anticipating the development of vitamin D toxicity. In some patients, the subjective signs of lassitude, anorexia, and so on appear early and are quite sufficient to warrant reduction of the dosage. Prolonged vitamin D intoxication will result in hypercalcemia and a condition comparable to hyperparathyroidism. The danger, of course, lies in the calcinuria which may injure the kidney. In such an instance, the glomerular damage could lead to retention, or elevation, of (acid) phosphorus (and nitrogen). While this might restore the level of phosphorus, it is accompanied by acidosis and the renal insufficiency. It can hardly be advocated as a controllable corrective measure.

DISCUSSION

The concept that resistant or refractory rickets is but an exaggeration of the vitamin D–deficiency rickets is controversial. Pedersen and McCarroll,[1] as well as Jonxis,[7] feel that the fault lies primarily with the metabolism of vitamin D rather than with the kidney tubule and with a tendency to persist into adult life as osteomalacia. Such factors as the familial and racial susceptibility may be found in both types, as is also the renal tubular loss of amino acids according to Jonxis.

Albright[11] ascribed the resistance to vitamin D "at the site where the vitamin had its primary action" (absorption of calcium from the gut) but also postulated a secondary hyperparathyroidism.

McCune[12] was one of the first to suggest that the primary defect in refractory rickets was in the renal tubular function. Obviously, all three—the metabolism of vitamin D, the parathyroids, and the renal tubule—may be involved but not necessarily as the primary or initiating factor. Fanconi[4] accepts the wide spectrum of renal tubular dysfunctions and coined the term "phosphate diabetes" for the severe refractory rickets.

Dent[2] differentiates more sharply the "phosphate diabetes" from the de Toni-Fanconi-Debre syndrome with its excessive amino aciduria and from the renal tubular acidosis (Lightwood's syndrome). Certain it is that the last type does not respond to vitamin D and requires compensatory administration of alkali.

While vitamin D in large amounts has proved useful in the treatment of some patients, the treatment leaves much to be desired in others. The response to high doses is not dramatic or as effective as is the vitamin treatment of vitamin D–deficiency rickets. The chronicity of most of refractory rickets and the persistance of the low-blood phosphorus of many patients into adult life prompts the search for additional measures. (Albright's[11] initial impression was that the condition was arrested at puberty with fixation of the epiphysea. While the phosphorus in the blood remained low and the phosphatase elevated, he considered the condition arrested or healed.)

Howard and associates[5] have studied the effects of infusion of calcium and conclude this results in the suppression of the parathyroid and, hence, the tubular loss of phosphate is reduced. The chain of events suggested is that, as in vitamin D deficiency, there is inadequate intestinal absorption of calcium which triggers the parathyroid activity. West, Dodge, and Daescher (Soc. Pediatric Research Abstract, No. 41, 1959), using phosphorus loading of patients with refractory rickets, conclude that, with vitamin D, the tubular reabsorption of phosphorus is normal. They find that less vitamin D is required and that, for the long term, treatment is more effective. Thus, these workers support the view that refractory rickets is not due to an intrinsic renal tubular defect. Fraser[10] and others found normal tubular function in patients given calcium infusion and vitamin D. Royer and associates,[6] in a study of 11 patients, concluded that patients with severe rachitic manifestations paradoxically respond to much smaller doses of vitamin D than do those patients with only moderate bone changes. With intravenous infusions of calcium gluconate, the retention of calcium was greater in the rachitic than in the normal controls, while phosphorus reabsorption was increased in the moderate rickets; the more severely rachitic who responded to the lower doses of vitamin D required long calcium infusions to obtain similar increase reabsorption of phosphorus. They have no explanation for the paradoxical differential in the moderate and severe rickets.

The author has tried a mixture of dicalcium phosphate (1 gm.) and sodium citrate (0.5 gm.) with the hope that the citrate might be of additional value since the diet, especially of American children, has usually ample, if not more than abundant, calcium and phosphate because of the high intake of milk.

On the other hand, Shohl and others, years ago, showed experimentally that the use of citrate, calcium, and phosphorus had a curative effect on vitamin D–deficiency rickets even in the absence of vitamin D. The citrate presumably facilitates calcium absorption from the gut, and it also is an important factor in the formation of the matrix receiving structure for the deposition of the bone salts.

If resistant rickets is but an exaggeration of vitamin D–deficient rickets, it might be expected to occur more frequently where deficiency of vitamin D is frequent. However, Mannerheim, who reports the high incidence of nutritional rickets in Abyssinia, stated emphatically that he found no increased number of resistant rickets in his extensive observations.

It is probable that there is more than one type of resistant rickets and that both theories are applicable. Since lead (heavy metals) and maleic acid poisoning will alter renal tubular function, some enzyme system or systems are probably involved. As such, a variety of conditions may produce temporary, acquired or permanent (and inherited) states of resistance to vitamin D. With one or more enzymes involved, vitamin D may be but one (coenzyme) factor of influence. The state of the parathyroid may also influence the effectiveness of vitamin D.

Stanbury[13] and others consider the pancreatic malabsorption syndrome a type of resistant rickets. While rarely seen in American children, celiac rickets has been recognized in England for some time. This condition also requires larger amounts of concentrated vitamin D and parathyroid enlargement suggests a secondary hyperparathyroidism.

Stanbury has also shown that the osteodystrophy associated with chronic renal failure, also called renal rickets, is associated with resistance to vitamin D and with secondary hyperparathyroidism. They have claimed benefit from massive doses of vitamin D and subtotal parathyroidectomy.

SUGGESTED STUDY OF RESISTANT RICKETS

Diagnosis. History. A family incidence of "bone disease" may be important. Delay in both physical and functional (that is, walking) development is a frequent finding. The nutritional or feeding history, especially of vitamin D, should be verified.

Physical examination. Widened epiphyses and bowing of the legs (especially in the older children) are characteristic. In addition, there may be enlarged costochondral junctures ("rosary") and bossae of the cranium ("hot cross bun head").

X-ray should demonstrate the swelling of the unmineralized epiphyseal osteoid tissue at the growing ends of long bones.

The laboratory should show changes in the blood calcium, phosphorus, and phosphatase. The most frequent is a low phosphorus and a high phosphatase. The urine should be examined for protein, sugar, and amino acids.

Treatment. If the patient is an infant, simple deficiency rickets will respond to 3,000 to 5,000 units of vitamin D with a return of normal blood values in two weeks time. X-ray may show deposition of calcium in the appearance of a white band at the growing ends of the long bones.

Resistant or refractory rickets will not respond to the low doses of vitamin D. The patient is started on 25,000 units of vitamin D daily. After ten days, the blood calcium, phosphorus, and phosphatase are repeated. In the absence of hypercalcemia, the vitamin D is doubled after ten days until 100,000 units per day are reached. At this stage, the patient is given increases of 25,000 units of vitamin D, continuing the tenth day check on the blood calcium and noting any subjective symptoms of hypercalcemia such as lassitude and anorexia.

For children three years or older, we may prescribe 0.5 gm. of sodium citrate and 1 gm. of dicalcium phosphate once daily, increasing as tolerated to three times a day.

Orthopedic bracing. Radical surgery is performed only after maturation (14 years).

RENAL RICKETS

In our experience, "renal rickets" is usually recognized or suspected in known patients with chronic renal failure. In these patients (polyuria, anemia, esthenia), the calcium may be low, and the blood phosphorus is usually elevated as is also the phosphatase. In addition, the blood urea nitrogen is increased, and acidosis produces a lowered base bicarbonate.

Treatment is directed toward reducing the phosphate load. While low (protein)-phosphorus diet can be tried, it is hard to maintain. Aluminum hydroxide (1 tbsp. t.i.d. p.c.) will greatly reduce the absorbable phosphorus in the digestive tract. Calcium lactate may be given (10 gm. daily), but care must be exercised in the use of strong alkalizing agents lest they precipitate tetany with convulsions. These patients will respond to increased doses of vitamin D and have, hence, been considered as having a type of resistant rickets. More basic to the correction of the fundamental pathology has been the successful transplant of normal kidneys. However, subtotal parathyroidectomy was necessary in one patient (McPhaul[14]) where renal transplant did not correct the hyperparathyroidism.

A rachitic condition of the bones may be found in association with renal tubular failure to reabsorb not only phosphorus but glucose and amino acids (Fanconi syndrome). Vitamin D is given to tolerance in these conditions. However, where the skeletal condition is associated with an acidosis due to the loss of fixed base or failure of amonia formation, or both, the administration of alkali is the effective therapy.

SUMMARY

1] There is a wide variation in the severity of resistant rickets. There may be several different causes and types.

2] The response to vitamin D varies between individuals and in the same individuals. This may be seasonal and related to sun exposure or there may develop an increasing antagonism to vitamin D.

(Metaphyseal dysplasia with hypophosphatasia presents the X-ray picture of resistant rickets but with normal levels of calcium and phosphorus in the blood. Healing takes place without massive doses of vitamin D. On the other hand, some patients with refractory rickets will demonstrate toxic symptoms with hypercalcemia before healing of the skeletal defect is evident.)

3] The use of additional calcium or phosphorus has been advocated. In some cases, it is possible that the alkalizing effect of added lime salts or with added sodium citrate (Shohl's mixture) favors deposition of calcium and corrects a latent or undetected acidosis.

4] A secondary hyperparathyroidism in resistant rickets as hypothesized by Albright[11] is rather widely assumed, but as yet there are no extensive reports on the effect of parathyroid removal. Frame reported one case which was not benefited by parathyroid removal. Stanbury[13] also considers the renal osteodystrophy another type of resistance to vitamin D in which massive doses are effective. Since Stanbury and, more recently, McPhaul and associates[14] have found beneficial results from subtotal parathyroid removal in the treatment of hyperparathyroidism secondary to renal disease, it might warrant more extensive trial in refractory rickets. Mc-

Phaul found that the evidence of parathyroidism persisted even after successful renal transplant had corrected the kidney dysfunction. From this, he suggests that parathyroidism had established a degree of autonomy and required subtotal removal for its correction. It is conceivable that there is a parallel situation in the severe cases of refractory rickets.

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Preventive Care of Infants and Children. VI:

School Adjustment Problems and Their Relationship to "Guided Growth"

BYRON B. OBERST, M.D.
Omaha

STEPPED-UP EDUCATIONAL PROGRAMS are bringing to view a number of children who are having difficulty in handling the work load or who are experiencing emotional upsets, as pointed out by Missildine.[1] Many of these children previously would have been overlooked or would have been conditionally promoted into succeeding grades. Teachers today are much more aware of the importance of recognizing immaturity, poor coordination, hyperactive behavior, and related factors; consequently, parents are being informed early of these problems and are seeking help for their children. A large segment of this group of children can be aided by today's medical approach which will lessen the financial and emotional burden on the family and the community.

This paper will describe one method of approach to this problem. The recognition, diagnosis, and treatment of school adjustment problems will be presented.

MEDICAL HISTORY

The history of a child, whether it be at the time of his preschool check at kindergarten time, at his yearly history review and physical examination, or at his presence at the doctor's office because of a school problem, should be reviewed for the following leading points and clues:

I. Past history and symptoms
    A. Severe colic
    B. Temper rages
    C. Marked breath-holding spells
    D. Accident proneness
    E. Convulsions, febrile or idiopathic
    F. Poor coordination
    G. Slow speech development
    H. Slow motor development
    I. Various schools attended by the child
    J. Different community school systems experienced by the child
II. Present history and symptoms
    A. Short attention span
    B. Poor concentration
    C. Hyperactivity
    D. Daydreaming
    E. Grades of less than potential ability
    F. Prolonged hostility
    G. Rebelliousness
    H. Irritating personality
    I. Frequent headaches
    J. Dizzy or light-headed spells
    K. Source of constant disturbance in the classroom.

Knowledge of the usual grades attained and the current report card status is very helpful. The change from a good performer to poor productivity is very significant. Trouble with arithmetic, especially in the thought problem area, gives insight into possible central nervous system disturbance. The easiest and hardest subjects should be ascertained. Homework habits, hours of study time, and bedtime hours give insight into a nonproducer or an individual who tries hard but finds the competition too difficult.

PHYSICAL EXAMINATION

The physical examination further pinpoints the areas of difficulty. Poor motor coordination[2] is the main area to examine. Rapid alternating hand movements, hopping on one foot, walking straight lines for balance, and drawing or writing with a pencil quickly uncover probable motor dysfunction. Body dominance may contribute to this difficulty.[3] If the child is left-eyed and right-handed or has other similar signs of mixed body dominance, these findings may be further evidence of motor dysfunction. Knowing the right hand and foot from the left hand and foot further pinpoints the knowledge of body dominance.

BYRON B. OBERST *is assistant professor of pediatrics, University of Nebraska College of Medicine, Omaha.*

Should there be adequate suspicion from the school performance record, history points, and/or physical examination, then a battery of diagnostic tests are very helpful in selecting the appropriate medications to assist the rehabilitation of the child. Because of the interaction of calcium, glucose, and thyroid in central nervous system growth, development, and function, the following tests are utilized: [1] six-hour glucose tolerance test to note for possible hypoglycemic reactions; [2] blood calcium and phosphorus; [3] kidney function and homeostatic control, blood sodium, potassium, carbon dioxide, chloride, and blood urea nitrogen; [4] thyroid function tests, protein-bound iodine and butanol-extractable iodine serum ratio, bone age, and, occasionally, the I^{131} uptake; [5] skull X-ray, anterior, posterior, and lateral, and electroencephalogram (EEG) with sedation; [6] blood pressure determination; and [7] I.Q. evaluation including gross I.Q., maturity level, and areas of specific school trouble. These tests may be accomplished in a thirty-six hour hospital stay, necessitating very little time away from home and school. The mother is instructed to call the office one week after the tests have been done for the report and interpretation of the findings.

SCHOOL RECORDS

To fully develop the all inclusive picture of the child and his problems, data supplied by a source agent are very helpful. A teacher or school counselor's report by telephone about the child's behavior in school, participation in class, and socialization develops an image of this child's activities. A letter to the board of education's special services division for the past educational difficulties adds scope and depth to the size of the particular problem. The school nurse, Visiting Nurse Association nurse, or public health nurse sees this child in different circumstances, and a home visit adds valuable information. The enlistment of help by the above people greatly aids the rehabilitation program.

PERSONALITY CLASSIFICATION

Children's personalities can be placed in one of four general classifications which is a help in understanding the child's response to his problem. These classifications are a modification of Barta's proposals:[4] [1] outgoing leader who usually has trouble with temper control and tact. This child becomes somewhat aggressive and ignores any criticism, [2] indwelling leader who usually is a "loner" and is not very cooperative. This child has trouble communicating and resents criticism, [3] outgoing follower who usually is a warm and affectionate child but is irresponsible and indecisive. This child means well but is ineffective and has trouble completing work, and [4] indwelling follower who usually is afraid to act, lacks self-control, and criticism crushes this child. Pressure is an item that is hard to tolerate. With the accumulation of the above data, a rational, intelligent approach to the individual child's problem can be assessed, a solution proposed to the parents, and, with their cooperation, therapy instituted with a good deal of hope for improvement in the child's future outlook.

MEDICATIONS

If any of the thyroid function tests are suggestively low, a six- to twelve-month trial of thyroid medication should be instituted to keep the level of the protein-bound iodine between 5 and 7 μg. The remainder of the medical approach is based on the EEG, the type of history presented, and the physical findings.[5]

1] An abnormal EEG with accompanying headaches, dizzy spells, or poor coordination receives a therapeutic trial of anticonvulsants based on clinical response. In order of preference by this author they are (a) reserpine products two to four times per day; (b) primidone (Mysoline®) 50 to 250 mg. two to four times per day; (c) diphenylhydantoin (Dilantin®) 50 to 250 mg. two to four times per day plus, occasionally, acetazolamide (Diamox®) 250 mg. two or three times per day; (d) phenobarbital ½ to 1 grain two to four times per day (this medication may make the child more irritable); and (e) occasionally, dextroamphetamine sulfate (Dexedrine®) 5 to 10 mg. per day.

2] A normal EEG with a history of short attention span and poor concentration receives a therapeutic trial of the so-called psychogenic energizers such as (a) methylphenidate hydrochloride (Ritalin®) 5 to 10 mg. two to four times per day; (b) acetamidobenzoate deanol (Deaner®) 100 mg. two to four times per day; and (c) dextroamphetamine sulfate (Dexedrine®) 5 to 10 mg. once a day.

3] A normal EEG with a history of hyperactivity receives a therapeutic trial of the so-called tranquilizers such as (a) reserpine products two to four times per day; (b) hydroxyzine hydrochloride (Atarax®) 10 mg. two to four times per day; (c) meprobamate (Equanil®) 200 to 400 mg. two to four times per day; (d) promethazine hydrochloride (Phenergran®) 25 mg. two to four times per day; and (e) trifluoperazine (Stelazine®) 2 mg. two to four times per day.

There may be a combination problem as evidenced by an abnormal EEG and hyperactivity and a short attention span, or both. If this problem presents itself, the first trial is with the anticonvulsants; if no improvement occurs, the tranquilizers then are used. Later, the attention span aspects of the problem are given the Ritalin®-Deaner®-Dexedrine® approach in combination with the other previously determined medication.

FAMILY CONFERENCES

The next step is the family conference, which is conducted in a peaceful and relaxed atmosphere, with both parents present. At this time, a short family personality profile is obtained. A determination is made of the father's and mother's respective roles in the family and the family philosophy and techniques of discipline. A deeper explanation of the hospital tests and the reason for the type of medication used also is given to the parents.

DISCUSSION

The aim of all pediatric programs is either the total prevention or early detection and correction of any problem.[6–10] A high index of suspicion in the preschool years concerning symptoms will lead to recommendations for the appropriate studies.

The single most important examination, after the first year of life, is the preschool examination for kindergarten. Not only should height, weight, and blood pressure measurements be done but also a Snellen eye chart, a hearing evaluation, and some simple coordination tests. These coordination tests can be finger-nose, rapid, alternating hand movements, and hopping exercises. Body dominance should be determined by eye-hand and foot usage. A simplified developmental test of visual and spacial appreciation can be done in a few minutes by having the child copy a circle, square, cross, triangle, and diamond and by drawing a man and a woman, or both. Fine finger coordination and maturity level can be fairly well assessed by the child's approach to this project.

The history at this interview should include salient personality points, socialization, and parents' feelings as to the readiness of the child for school. The immature child, the extra-young child, or the indwelling, poorly socialized child may need to be retained from school for another year and helped with his problem.

The particular personality guidance advice concerning the involved child obviously is dependent on the type of personality he presents so that undue pressures, criticisms, frustrations, and rejections are avoided. The atmosphere at home needs to be one of willing cooperation and support of the child's difficulty without overprotection.

The mother is requested to report at weekly or biweekly intervals the child's response to medication as exhibited by his behavior. This can be done by short phone calls during office hours so the child's chart will be available for reference. The teacher is requested to make similar reports on classroom behavior and endeavor at two- to three-week intervals. These calls are usually made at the teacher's convenience, but during office hours so notes can be made on the child's chart. These reports help to determine the effectiveness of the therapeutic program and indicate any necessary changes. The child is checked in the office every one to three months, depending on coordination problems or other areas of difficulty. This entire program does not entail a great outlay of time by the busy practitioner and can be done successfully without the great number of multipersonnel conferences so much in use today.

After the first grade, all children's annual physical review should include a simple reading test such as the Gray's Oral Reading Paragraphs and, after grade three, a written spelling test for the appropriate grade as obtained from the World Book Encyclopedia or other source material.

The information obtained each year regarding the child's easiest and hardest grades and his best-liked subjects helps to determine his response to school and, in addition, allows an opening for discussion of difficulties with the parents if there is an apparent need. Potentially gifted children may be suspected and uncovered in this manner, as an added dividend, and helpful advice can be given to the parents regarding the child's future needs.

The greater the liaison and cooperation between the fields of medicine and education as a whole and the physician and the teacher individually the greater the opportunity to lessen the appalling school failures, school dropouts, and mental or physical problems this country is experiencing. This especially is true of the potentially above-average student who constitutes such a waste of human capabilities.

SUMMARY

Stepped-up educational programs are revealing a number of children who are experiencing emotional upsets and problems or who are having difficulty handling the school work load. Many of these children can be helped by today's medical approach. The recognition, diagnosis, and treatment of school adjustment problems are discussed. The importance of a complete medical history and examination and the need for close cooperation with teacher and school regarding the child's progress are explained. The selection of the therapeutic regimen is given together with follow-up procedures, preventive measures, and early means of detection of problems.

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Gastrointestinal Disorders and Developmental Stress in Childhood

RICHARD L. COHEN, M.D.
Omaha

INTRODUCTION

The gastrointestinal tract is intimately tied to dependency gratification, tension reduction, and impulse expression. For this reason it assumes a position of primacy as an organ system for psychosomatic disorders during infancy and childhood.

In attempting to understand the genesis of these conditions, we have found the conventional model of illness—that is, one or more noxious agents producing structural damage and malfunction—less useful. We have also lived through a period of attempting to understand the various psychosomatic diseases occurring respectively in specific types of personality profiles.

Classifications based on these concepts have some validity but tend to break down in practice because of the great number of exceptions to them. It seems to make more diagnostic sense and provide a more rational basis for management to consider the various disorders as body efforts at adaptations to stress; that is, to view them as patterns of reactivity or responsivity to stimuli which are threatening to the psychosomatic integrity of the individual.

Perhaps another way to say this is that we are all familiar with the receptive capacities of the gastrointestinal tract; what we need is more knowledge of the gastrointestinal tract as an organ system of expression or interpersonal communication.

Our ability to classify psychosomatic gastrointestinal disorders in children is enhanced if we conceptualize them in terms of adaptive reactions to developmental and situational stresses occurring in certain patterns. It can be demonstrated that these are not independent clinical entities with grossly different etiologies which happen to appear in the same organ system. On the contrary, their occurrence in the gastrointestinal tract is associated with the function of that tract in the developing human organism.

ADAPTATIONAL APPROACH TO GASTROINTESTINAL DISTURBANCES

In order to place these disorders in the proper frame of reference, it may be helpful first to consider what the broad developmental tasks of childhood and adolescence are. There is evidence to indicate that it is in relation to these developmental tasks, that many psychosomatic disturbances evolve. One way to look at the human growth process in its broad outlines would be as follows:

1. During the initial period beginning with birth and for the next days or weeks, somatic survival of the organism is the primary task of life.

2. Following this initial period of highest somatic vulnerability, the next adaptations for the infant involve capacity for self-organization on a physiological and behavioral basis. Through the developing social tie with the mother, there is increased capacity for tension bearing and eventually, socially acceptable tension discharge. This displays itself in such phenomena as the ability to sleep all night and to settle down to a fairly regular schedule of feeding, sleeping, and elimination.

3. This leads to a period of several years of effort at achievement of increasing states of autonomy and capacity for separate function from the nurturant adults in the child's life. This is seen especially around capacity for self-care, toileting, dressing, and most importantly, the capacity to go to school in a separate environment and function independently in a group not responsible to the parents.

4. This should all be accompanied by increasing achievement in another area of adaptation having to do with social cooperativeness and the

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RICHARD L. COHEN *is associate professor of neurology and psychiatry, University of Nebraska College of Medicine, Omaha.*

ability to form warm, stable, give-and-take relationships. The child's ability to identify with a peer group, to accept group goals, and indulge in group efforts is vitally important to the achievement of eventual adolescent and adult status.

For a variety of reasons, some children find that the achievement of one or more of these adaptational goals so overwhelms their usual mechanisms to cope with stress that they must resort to the use of psychosomatic defenses. In children, perhaps, this is seen most clearly and dramatically in the gastrointestinal tract.

If one re-examines the various syndromes which have been described in this somewhat different frame of reference, they begin to become more understandable.

It is understood that these are not discrete periods of development in the human organism occurring in a straight-line chronological course, but that, to a large degree, they occur concurrently and achievement of one set of adaptational goals is influential in the manner in which another set is achieved.

SOMATIC SURVIVAL

We have learned from the work of Spitz,[1] Bowlby,[2] and much of the ethological research[3-5] done in the past fifteen or twenty years, that there is a significant relationship between the manner in which the infant makes a social tie to the mother and the manner in which it deals with the most primitive forms of stress. The need for timely and appropriate stimulation, maternal ministrations which are tension relieving at other points, and maternal behavior which is predictable, stable, and consistent has been demonstrated to be crucial to the capacity of the infant to survive and, subsequently, thrive. The so-called "failure to thrive" syndrome would seem to represent a situation, in the absence of gross organic damage in the infant, in which the child has not made an adequate social tie to a stable maternal figure which is perceived by the child as being nurturant. Any factors which interfere with the formation of this tie may present the child with such overwhelming stress that he may need to resort to "self-nurturant" behavior in order to survive. It may well be that some of the gastrointestinal syndromes seen in infancy represent effort in this direction.[6,7] In this instance, we would describe the adaptational mode which was operating as "restitutive behavior." An example of such a disorder is rumination.

CASE REPORT 1

A 9-month-old male was delivered at thirty weeks' gestation with a birth weight of 4 lb. 5 oz. The 38-year-old mother, recently married after a brief courtship, did not believe she would ever marry. Her pregnancy was free of health contingencies but she was depressed and anxious because she felt unattractive to the husband four years her junior.

Postnatally the infant progressed slowly though the general, overall condition was satisfactory. He required a three and one-half week nursery stay. During this time the mother was home alone with little to do. She felt detached and "unemotional" about the baby. During this period she discovered that her husband was engaged in an extramarital affair.

When the baby arrived home the mother gave good physical care but was very depressed and would sit for hours crying, sometimes while she was actually holding the infant in her arms feeding it. The husband was rarely at home.

At about 4 months the infant seemed restless and fussy and began to regurgitate after feedings. Soon after this he seemed to be able to do this voluntarily, going through motions of mastication and then reswallowing food. This continued with increasing frequency over the next several months. The fussiness stopped but the infant became more removed and unresponsive and showed little interest in surroundings.

More detailed interviewing of the child's mother in this case indicates that her depression during the pregnancy was exaggerated by the discovery of infidelity in her husband during the period of the child's postnatal hospitalization. Experience with premature infants[8] indicates that it is difficult under the most normal of circumstances for the mother to maintain an emotional tie to the infant when she has never cared for it and when there is a prolonged period of separation following birth. Our experience in this case strongly suggested that the mother was not psychologically available to the child despite adequate physical care which she rendered. The child's buildup of discomfort during the weeks following his entry into the family seemed eventually to have been handled through isolating, autoerotic behavior primarily centered in the gastrointestinal tract.

SELF-ORGANIZATION AND TENSION HANDLING

The undifferentiated discharges of tension displayed by infants during the first few weeks of life tend to become more organized and more highly differentiated as the child develops a tie to the mother. It is through the organized behavior of the mother and the child's ability to internalize an image of the mother which is comforting and supportive that the environment contributes most heavily to the child's growing self-organization. It would appear that in situations where there is not a stable maternal figure, where the environment may be highly tension relieving, or where the mother's care has a paradoxical or inverse value toward the infant—maternal behavior designed to reduce tension actually increases it—that we may tend to see the child resorting to gastrointestinal mechanisms really designed to reduce tension in another fashion.[9] Under the circumstances the adaptational mode may be described as "somatic tensional discharge."

There is evidence to suggest that such syndromes as colic and persistent vomiting in infants actually represent efforts to handle tension states through somatic discharge.[10] The following case may illustrate this point.

CASE REPORT 2

A 4-month-old girl was cared for in the home of her paternal grandparents. She was the first child of an 18-year-old mother living with her in-laws while her husband was overseas in military service. The mother was depressed and anxious over the separation from her husband who was 19 and the oldest of 7 children. His siblings ranged in age from 7 to 17 and all lived at home. The mother, paternal grandmother, and father's siblings all alternated in caring for the baby without any fixed or predictable pattern. The baby was handled and fondled continuously and was everyone's "pet puppy" (mother's words). The house was crowded, noisy, and filled with constant physical activity. Within two weeks the baby was vomiting in connection with each feeding, either during a meal or shortly thereafter. Food spurted and was often projectile in nature. This was handled by refeeding. There were no gross physical findings in the child including a complete neurological work-up.

This type of case should be differentiated from those described in the first category because it seems clear that the child received a good bit of emotional stimulation, lived in a climate in which she was highly valued, and enjoyed considerable emotional interaction with the adults. This type of psychosomatic response seems to be a relatively undifferentiated one in contrast to some of the disorders described below.

STRIVING FOR AUTONOMOUS FUNCTION AND SEPARATENESS

When the child has achieved adequate stability physiologically and behaviorally and is sufficiently organized to begin exploring reality and learning the skills of self-care—and subsequently, the gratifications of productivity—he faces additional adaptational stresses. These particular stresses are not confined to childhood exclusively but may appear all through life. However, the initial experiences with achieving autonomous function and separateness from parents are usually the most stressful, and if there is impending failure of the child's abilities at this point, he may begin reaching out to the parent in a fashion which denies the separation and seeks to maintain the symbiosis of early childhood. A common avenue for the expression of such defenses is through the gastrointestinal tract. We might say that under these circumstances the adaptational mode is represented through "regressive behavior." Examples of this type of gastrointestinal syndrome can be seen in the chronic abdominal pain, often accompanied by diarrhea, which may be associated with school avoidance.[11] It may very well be that anorexia nervosa itself is an example of this category occurring in adolescence. The following case illustration may be useful for clarification.

CASE REPORT 3

A 7-year-old girl in second grade resisted going to school in the morning. Intermittent bouts of diarrhea and abdominal pain occurred for five months. Hospitalization on a pediatric ward for ten days revealed no physical abnormalities. The child was the middle of 7 children in a family with marginal finances. There had been multiple health contingencies in children and parents since before the birth of the patient. However, the girl herself had always been in excellent health. Described as an "itch" by her mother, she was a demanding, provocative child who was especially rivalrous with her next youngest female sibling. This sibling had contracted rheumatic fever eighteen months before the onset of our patient's symptoms and had required much special attention and care. During the fall of the patient's second school year she developed what seemed like a common viral enteritis. This lingered with much cramping, low grade fever, and moderate bouts of diarrhea. On each occasion, she dramatized her symptoms, clung to mother, and refused to go to school.

One of the child's first experiences with dependency gratification, of course, is in relation to needs met through the gastrointestinal tract. It is logical to assume that under conditions which may overwhelm the child's capacities for independent action, that he should resort to regressive maneuvers expressed through the same organ system. In anorexia nervosa, where the child seems to be struggling with pressures for autonomous function on still a more mature and separate level, it would seem that the defenses need to become more extreme, the denial of the separation more total, and the resistance to both more heroic.[12]

STRIVING FOR SOCIAL COOPERATIVENESS AND RELATIONSHIP FORMATION

The achievement of an adequate social tie to the mother with subsequent achievement of autonomous self-care, exploratory behavior, and reality testing permits the child to develop other relationships outside of the original mother-child axis. If these initial goals have been achieved to an adequate degree, there will be sufficient trust in the formation of other relationships and in the yielding of some independence to the group so that identification with group goals and group standards is possible. One sees the child moving from isolated play to parallel play and, finally, to interactive, socially cooperative play as he proceeds through the preschool years and approaches participation in a formal school group. As well described by Erikson,[13] the child's capacity to develop this state of trust in the reality and value of his own emotional life and that of others makes relationship formation possible and desirable. In situations where the child has learned to distrust his own emotional responses to other people or where he has learned that certain kinds of emotional responses are highly unacceptable—even catastrophic—to the adults in his life, he will need to develop personality defenses which permit for social isolation and the repression and denial of these affects. Again, what we see is that certain children need to reach for psychosomatic mechanisms in order to deal with the stress involved. It appears that the lower bowel has become associated with this type of disturbance. Within this group we would put such syndromes as encopresis and ulcerative colitis. The basic adaptational mode operating in these disorders would be "somatization of unacceptable affects." This is to say that the child handles his emotional life in relation to significant adults by choosing symptoms which may tend to isolate him from further intimate social interaction and yet which, at the same time, tend to act out or express in body language those very negative affects which are so ego dystonic to the parties in the interaction.[14] The following example is illustrative.

CASE REPORT 4

A 4-year-old boy had persistent constipation and fecal soiling. The father was a young intellectual lawyer and the mother was the youngest child in a family where she was highly indulged and infantilized. She called her mother and older sister on the telephone several times a day "just to talk to them." The latter two women were critical of her child caring ability and practices and she leaned over backward to please and impress them without ever really achieving this. The patient was described as having been a "sluggish" infant, but ate well and was in good general health. He often went two to three days without a stool and the mother began a regime of daily enemas and suppositories or both, despite advice of the family physician that this was normal. Toilet training began at 10 months. The child spent long hours on the potty until he produced a stool. Daily activity began to center more and more around the child's bowel movements or lack of them. He began to complain of pain at stool and inability to defecate. With longer periods of constipation, the mother became more upset and began to "shop" from doctor to doctor demanding medication that would insure normal bowel function. By the age of 3½ the child was soiling daily and constantly had a fecal odor so that he was rejected by his peer group in nursery school. The boy showed no apparent concern about his soiling.

Our findings concur with many reports[15,16] which have noted that in these families negative or separating affects are intolerable and the child develops little comfort with them. They may appear as temper tantrums at times early in development but eventually one tends to see a superficially conforming, passive child who simultaneously expresses his hostility and his resistance to control by fecal withholding and soiling which makes him increasingly socially unacceptable.

IMPLICATIONS FOR CLINICAL PRACTICE

The basic purpose of this paper has been to invite the physician's attention to the defensive nature of functional gastrointestinal syndromes in childhood. The advantage in conceptualizing these disorders in this way is that they become more meaningful in the total context of the child's life situation and are not simply viewed as disease entities apart from the child's developmental process. This allows for more rational therapeutic planning for the child. If the physician is able to identify specifically those adaptive tasks with which the child is struggling unsuccessfully, he may then be able to place himself in a position within the case to be more helpful both to the parents and child in supporting and stimulating the child's growth process.

The 4 categories described above cannot be all inclusive and, of course, situations arise which represent growth failure in other areas, or even some combination of the above syndromes.

Nevertheless, if the physician uses this categorization as a departure point, he may then view the various syndromes involved as representing problems in one of the following areas: (1) somatic survival, (2) self-organization and tension management, (3) autonomous function and separateness, and (4) social cooperation and relationship formation.

He will then also be able to recognize that the adaptive capacities of the child need some combination of medical, social, and parental support dictated by the specifics of the situation. It is difficult to see why the child with encopresis requires a different kind of management than the child with functional abdominal pain without this kind of orientation.

Therapeutic approaches based on the child's presenting symptoms may not only be useless, they may be harmful in the sense that eventually they may contribute to the chronicity of the problem by supporting the parents' impression that the basis for the difficulty is indeed in the gastrointestinal tract. It is as if the parents are helped, in these situations, to deny the interpersonal aspects of the child's disorder and to constantly search for some simple and specific procedure or drug to alleviate the child's difficulty.

Furthermore, temporizing phrases such as "He will outgrow it" may give temporary reassurance but may also contribute to chronicity if the condition is not truly one which is a transitory developmental deviation within normal limits.[17]

The model of medical care suggested by the concepts in this paper is one in which the physician attempts, early in the case, to identify (1) the assets and liabilities in the child and family for producing favorable developmental outcome in the child, and (2) the specific nature of the adaptive task with which the child is struggling and the nature of the compensatory psychosomatic defenses which have been called into play (such as restitutive, regressive, tension discharging, or somatizing).

This information, if acquired in an organized and structured fashion early in the child's treatment, will point to treatment strategies which go far beyond the management of the diarrhea, vomiting, or other specific, presenting complaints. For instance, it may be that instead of resorting to frequent formula changes in a 3-month-old infant with paroxysmal fussiness or colic, the treatment may actually involve counseling of the inexperienced or overanxious young mother, advising changes in the living habits of the family, providing for periods of buffering between mother and child, and using mild tranquilizing agents in one or both in the hope of increasing the threshold to noxious stimulation.

It may be, in other instances, that exploration of the child's socially interactive behavior, his attitudes toward separation from the family, and his image of himself as an individual with a specific sexual identity may suggest such malignant personality stresses at work as to warrant a referral for psychiatric care quite early in the case. It has been suggested by many observers that such conditions as ulcerative colitis, regional ileitis, and anorexia nervosa actually represent defenses of psychotic proportions appearing in somatic form.

In any event, treatment strategies should begin to take the form of fostering adaptation to developmental stresses in the child rather than restoration of somatic homeostasis.

SUMMARY

A schema for viewing functional gastrointestinal disturbances in children within the framework of the child's total developmental process has been presented. It is suggested that these disturbances represent a variety of efforts at compensating for partial or total failures with stress coping at several levels.

It is suggested that rational therapy depends on the capacity of the physician to view these disorders in interpersonal terms and within the total context of the family's child rearing resources at the moment. The role of the physician in treatment then becomes one in which he serves as an agent to support those resources which may be deficient to foster the child's adaptations to stress.

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Psychological Variations in Patients with Gonadal Dysgenesis (Turner's Syndrome)

Report of Two Cases: Role of the Medical Genetics Counselor

HENRY T. LYNCH, M.D., THADDEUS P. KRUSH, M.D.,*
and ANNE J. KRUSH, M.S.
Omaha

ROBERT L. TIPS, M.D.
Houston

The striking phenotypic findings in patients with gonadal dysgenesis (Turner's syndrome) rarely present any diagnostic difficulty.[1–4] However, patients with this condition may show profound psychological differences conditioned, in part, by their endocrinologic and phenotypic peculiarities.

The purpose of this report is twofold: [1] to describe two patients with gonadal dysgenesis who were phenotypically very similar but who differed remarkably in their psychological reactions, and [2] to point up the need for physician-oriented genetic counseling utilizing a team approach to meet the manifold psychological and medical needs of such patients.

MATERIAL AND METHODS

Two patients with gonadal dysgenesis and key members of their families were investigated intensively at the University of Nebraska College of Medicine. Detailed physical examinations including electrocardiograms and X-ray studies were performed. Leukocytes were cultured for chromosome studies. Each patient was seen by members of the psychology department of the Nebraska Psychiatric Institute, where a battery of psychological studies was performed including the Wechsler Adult Intelligence Scale, the Draw-a-Person Test, the Face-Hand Double Simultaneous Stimulation, the Benton Visual Retention Test, and the Thematic Apperception Test. Interviews were conducted with the patients and the immediate members of their respective families by an internist-geneticist and a medical social worker. Each patient was interviewed in turn by a psychiatrist.

CASE REPORTS

Case 1. E.V. is a 43-year-old white woman who was seen at the University of Nebraska Hospital because of hypertension, severe generalized headache, and hypothyroidism. Medical history revealed that a physician, on the basis of her appearance, concluded that she was "obviously hypothyroid" and instituted therapy with thyroglobulin (Proloid®), 5 to 9 gr. daily over a six-year period. Our studies indicated that, in fact, she was not hypothyroid but that her gland became suppressed by the exogenous thyroid administration. The details of this are the subject of another report.[1] The diagnosis of hypertension had been established at age 22 and she had been controlled on several medications, the most recent of which was hydralazine hydrochloride (Apresoline®). She admitted to having been "heavy" all of her life. She had never menstruated, and her breasts had not developed. A scanty amount of pubic hair appeared at age 15, but no axillary hair had grown. The remainder of the medical history was noncontributory. Pertinent psychiatric history revealed that the patient had never dated or experienced libidinal drive. Additional psychiatric history and findings will be discussed.

Physical examination showed the patient to be obese;

HENRY T. LYNCH *is instructor, Department of Internal Medicine, Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska College of Medicine, Omaha;* THADDEUS P. KRUSH *was professor of psychiatry, University of Nebraska College of Medicine, Omaha;* ROBERT L. TIPS *is assistant professor of pediatrics, Baylor University College of Medicine, Houston; and* ANNE KRUSH *is an instructor, Department of Internal Medicine, University of Nebraska College of Medicine, Omaha.*

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*Deceased October 19, 1965

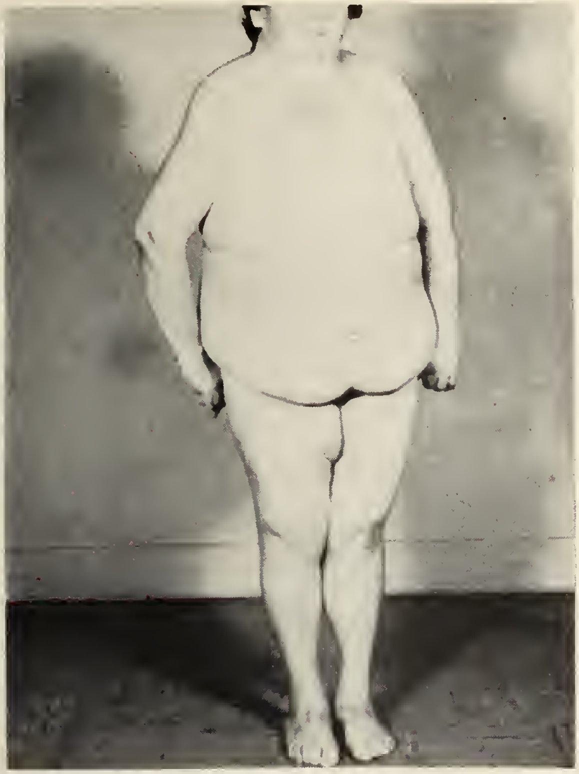

Fig. 1. Patient E.V., with the characteristic phenotype of Turner's syndrome

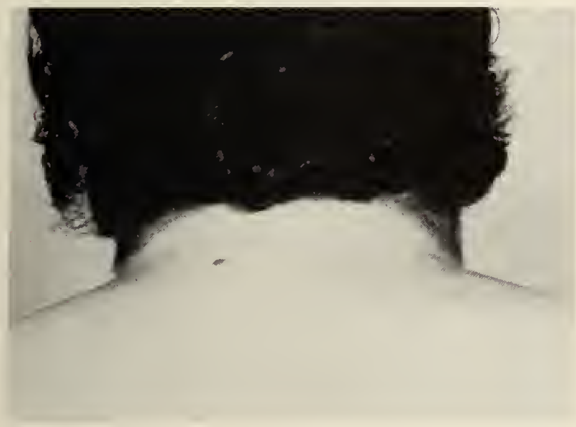

Fig. 2. Patient E.V., showing the short neck and low hairline

she had a broad, dull facies, pterygium colli deformity, shield-like chest with widely spaced nipples, and short hair line (Figs. 1 and 2). Her height was 5 ft. and her weight was 175 lb. Blood pressure in the right arm was 190/96 mm. Hg, with similar recordings in the other extremities. She had a high-arched palate and funduscopic examination revealed a grade 2 hypertensive retinopathy. Examination of the heart showed a grade III to VI harsh systolic murmur, loudest over the aortic area, which was transmitted into the neck bilaterally. Genitalia were infantile with scanty pubic hair. The remainder of the examination was within normal limits.

Laboratory studies. Complete blood count, urinalysis, blood urea nitrogen, and electrolytes were within normal limits; urinary steroid excretion studies were normal. A four-hour oral glucose tolerance test was distinctly abnormal, being compatible with diabetes mellitus. A protein-bound iodine test was 1.9 μg. percent, with normal values appearing approximately three months after withdrawal from exogenous thyroid medication. A chest X-ray showed cardiomegaly with left ventricle prominence and there was a positive metacarpal sign. A karyotype analysis showed 45 chromosomes of the characteristic XO pattern (Fig. 3).

Psychological studies. On the figure drawing test, when asked to draw a human figure, E.V. drew an empty box-like figure without hands or facial details. Asked, "Is it male or female?" she replied, "Either." On a forced choice, she indicated that it was a male. Asked to draw a female, she drew a second figure which was almost identical with the first, modified very slightly in the chest section, presumably representing breasts. Her visual organization score of 21 correctly identified objects out of 30 suggested mild impairment in visual organization. Severe impairment of visual retention was indicated in a score of only 2 correctly reproduced Benton visual designs. WAIS measures of intelligence showed the following I.Q.s: full scale 86, verbal 94, and performance 77. Projections in the Thematic Apperception Test reflected concrete mundane fantasies that were unremarkable except for the following responses: [1] somebody taking something from someone that belonged to her which she did not want that person to take (said twice) and [2] someone looking for a thing or someone "and if it's there, she'll find it." Asked what the thing was and what was going to happen, she replied, "She wanted that thing or someone. Could be a person, sewing material, furniture. If it's there, she will find it."

Interview. The family history revealed that E.V. had 5 siblings, all in good health, and none with a condition similar to hers. Her father and paternal uncle had expired from carcinoma. Her mother was healthy at age 70, and a maternal aunt had expired from diabetes mellitus at age 60. No history of gonadal dysgenesis was found on either the maternal or paternal sides of the family. General questions were then asked to obtain information concerning her own self-image, her feelings toward her family and peer group, and her interests in the opposite sex. She stated that her entire life was cen-

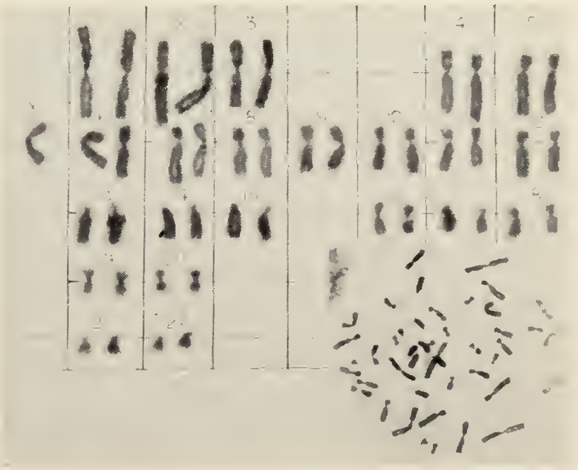

Fig. 3. Karyotype of a cell on patient E.V., showing chromosome count of 45 with the XO pattern of Turner's syndrome

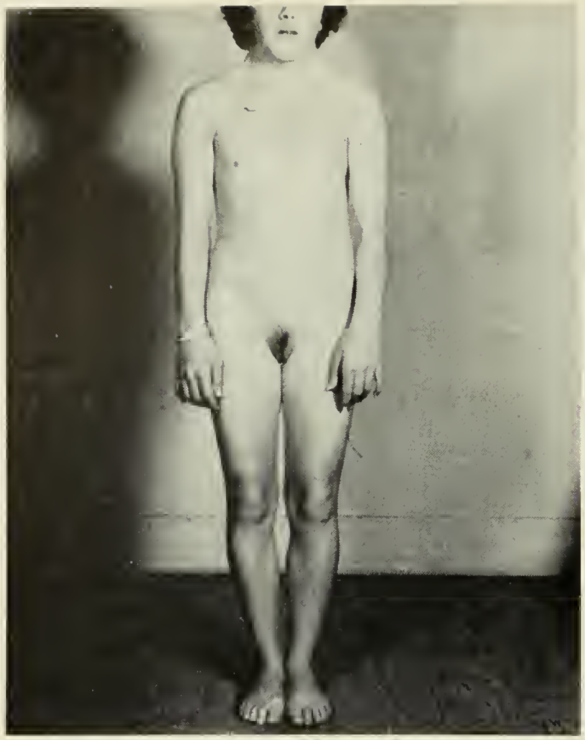

Fig. 4. Patient P. E., with the characteristic phenotype of Turner's syndrome

tered around her family and her mother in particular. She made many references to her love and affection toward her mother and felt that this love was reciprocated by her mother, sisters, and brothers. Her profound allegiance to her mother was seen when she was asked if she ever smoked or drank and she replied unhesitatingly that her mother did not approve of this and she would never think of doing anything without her approval. Responses to questions about relations with her peers suggested that she felt that everybody liked her "because I like everybody." She could not recall one single instance where people made fun of her because of her appearance but she appeared to be evasive on these latter points. She blocked considerably on questions of dating and stated, "It is just one of those things." On further questioning along these lines, she indicated that men did not mean anything to her and that she had never had any interest in them.

Case 2. P.E. is an 18-year-old white female with a previous diagnosis of Turner's syndrome. In 1959, she underwent a thoracotomy for correction of coarctation of the aorta. She was amenorrheic, and her secondary sexual development was severely retarded. The remainder of the medical history was noncontributory. Pertinent psychiatric history indicated great wishes to "be like my sisters and other normal women." She repeatedly talked of her interest in boys and her hope that some day she would marry and have children.

On physical examination, this patient appeared to be about 12 years of age rather than her chronologic age of 18 (Fig. 4). She was 4 ft. 6 in. tall and weighed 85 lb. Blood pressure was 110/60 mm. Hg in the right arm, with similar recordings in the rest of the extremities. There was a high-arched palate and the pterygium colli was prominent. She had a shield-like chest with widely spaced nipples and undeveloped breasts. There was a minor degree of pectus excavatum; there was scanty pubic and axillary hair, and the genitalia were infantile. The remainder of the physical examination was within normal limits.

Laboratory studies. The urinalysis, hemoglobin, complete blood count, fasting and two-hour postprandial blood sugar, and blood urea nitrogen were all normal. X-rays of the hands revealed delayed fusion of the epiphyses of the ulna and radius. The metacarpal sign was absent. Karyotype analysis showed a chromosome count of 45 with the characteristic XO finding of Turner's syndrome (Fig. 5).

Psychological testing. The patient was attentive, alert, and cooperative throughout the testing situation. Her intelligence (full scale I.Q. 82) was in the dull normal range and commensurate with her educational background (completed eighth grade). She said that there were 64 weeks in a year and described Longfellow as a pirate, suggesting a limited amount of early learning and a restricted cultural environment. Attention span and auditory memory, or both, were markedly subnormal. However, practical social intelligence as measured by the comprehension subtest was slightly above the normal range.

Average intellectual endowment was also indicated by her scores on picture completion and block design. There was no evidence of marked cerebral dysfunction characteristic of brain damage. All 10 double simultaneous face-hand stimulation were correctly identified. Her score on the visual organization test (24 out of 30) was only 1 point below the lower end of the normal range.

The personality projected in figure drawings and in the Thematic Apperception Test was immature and pertaining to sexual identification was unremarkable. During interview, she responded to questions with embarrassed smiles and laughter. She said she hoped to be married like her sister and have babies.

Interview. The family history was reviewed privately with the proband's 2 sisters and with her mother. There was no evidence of any other cases of Turner's syndrome in the family, and examinations of the above relatives failed to reveal any stigmata of this condition. Each of these individuals related a similar history, portraying the subject as shy and self-conscious about her condition. They pointed out that, from their earliest remembrances, she was teased by her peer group because

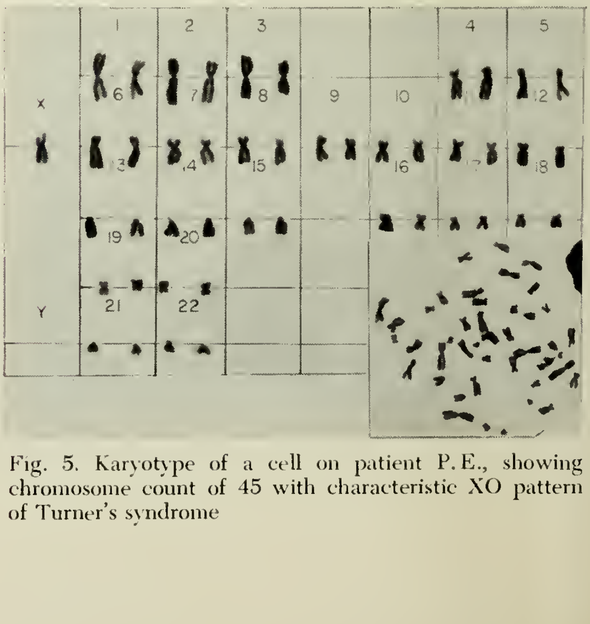

Fig. 5. Karyotype of a cell on patient P. E., showing chromosome count of 45 with characteristic XO pattern of Turner's syndrome

of her markedly short stature, webbed neck, and peculiarly shaped ears. The latter finding gave rise to the term "rat ears," which even her own brother frequently called her. She never reacted to these epithets but, rather, always "kept things to herself." The only one in the family in whom she confided was her older sister (4 years older), now married with 2 children. To this sister she revealed her great concern about her absence of sexual maturation "like other girls do." She started to talk about this at the age of 14; her concern mounted, and she began to show great anxiety. Frequently, she asked her sister if she would ever have dates and if she could have babies. She spent considerable time caring for her sister's children, "playing mother," and expressing the hope that she might some day have babies "just like my sister's." The sister never answered the question relevant to her capacity to have babies. "I wasn't sure myself . . . but I do remember a doctor telling Ma and me that 'Sis' could never have any babies."

Interview with the patient revealed her to be attractive and neat, with well-groomed hair. She was shy, talked of her problems in a superficial way, and stated that she had hopes of being "different" (more like a girl) as a result of the medications (estrogens). She hoped that some day she would become more attractive to boys and eventually would marry one and have babies. After estrogen therapy was started, she experienced "break through," monthly paravaginal bleedings, and, according to both her sister and her, she became elated, with considerable gain in confidence. However, she began to miss clinic appointments and the estrogen treatments were stopped. Likewise, the "break through" estrogen response ceased. This became a shock to the patient; she became depressed, crying frequently and uncontrollably, and manifested insomnia. It was during this time that we hospitalized her and were able to observe this behavior.

DISCUSSION

During embryogenesis, the undifferentiated gonad is believed to be directed toward predominant medullary development with testes formation when a Y chromosome with its male sex determining genes is present; conversely, the presence of 2 X chromosomes favors the predominance of cortex development with resultant ovarian formation. However, the XO (absence of a second X or Y chromosome) state of gonadal dysgenesis appears to be a unique one. The product is a phenotypic female with fibrous gonadal streaks in the broad ligaments and histologic absence of clear-cut male or female features.[4] While the mentioned phenotype is designated female, in the strict sense, this is only partial female. It portrays an amenorrheic individual with infantile genitalia, absence of breast development, scanty pubic hair, often absence of axillary hair, lack of feminine delineation, and associated grotesque features, that is, webbing of the neck, hypertelorism, genu valgum, and shield-like chest. With such marginal and ambiguous anatomy, how does one identify?

There is a marked paucity of literature treating the psychiatric aspects and, more particularly, the sexual role of patients with gonadal dysgenesis.[5] One report showed a patient with this disorder who developed schizophrenia,[6] while a second case report described one who developed anorexia nervosa.[7] In a study of identical twins with gonadal dysgenesis,[5] one twin showed rather positive interests in the opposite sex while her co-twin was indifferent. The authors concluded that ". . . it would appear that interactive roles of chromosomal phenotype and environment factors in psychologic sex determination deserve further research and clarification, particularly in connection with sexual drive.[5]" This observation was in contradistinction to that of Hampson and associates[8] who felt that ". . . a person's conviction of himself as a man or herself as a woman—the gender role and erotic orientation—is a variable quite independent of genes and chromosomes.[8]"

Sabbath and associates,[9] in a study of 7 adolescent girls with ovarian dysgenesis, found that their major concern pertained to their markedly short stature. Lesser, but also significant, concern was expressed about their sexual and reproductive function including menstruation. Three of the 7 girls were concerned about their unfeminine appearance, while 4 expressed no interest in female development or function. The personalities of their mothers were especially important in influencing the adjustment of these girls. The authors emphasize the importance of psychiatric consultation before the start of hormone therapy to help the patients accept such estrogen therapy with its resultant "menstruation."

In this paper, 2 patients with Turner's syndrome with phenotypically similar features were shown to differ remarkably in their respective identifications. One of these patients (E. V.) was strikingly neutral and denied ever experiencing libidinal urges. She had directed her entire energies into a role of subjugation to her mother, with a staunch desire to reap love from her siblings and other family members. This appeared to be her sole motivating force, and she appeared to be fully gratified in this role.

In contrast, the second patient, with the same condition and similar phenotype, seemed to have a slightly different self-identity and frame of reference. Limited libidinal drive was expressed as a wish to be like her sisters, to have babies, and to go out with boys. However, there was no evidence of libidinal drive in the form of erotic expression toward herself, her sisters, or boys. Thus, one must postulate her sexual identification as neutral, with external forces pushing her toward being female. Acceptance of herself as she is leads to apathy on her part as to outcome. This general theme was found throughout the interviews and was corroborated in psychological testing.

The presentation of each of these cases to the medical genetics counselor poses unique problems which obviously cannot be answered by a mere chromosome interpretation.

The emotional reactions of both of these patients are deep seated, and our studies have only touched upon the surface of their myriad problems. The nature of the problems in each patient, however, pertains to a sexual role and the question is raised: How does one with an ambiguous anatomic phenotype and an aberrant endocrine system relate to this role in accordance with society's dictum as to what constitutes a male and a female? Certainly, the absence of a penis and the presence of a labia majora, no matter how rudimentary, prompts the parents to impose a feminine role upon such patients. However, the phenotypic appearance of such patients is not conducive to sexual affective attention by the opposite sex. The sexual dilemma is between female and neuter, not between male and female. Our 2 patients would appear to react to this by differing defense mechanisms. The first patient continually expressed feelings of indifference toward men and showed great indulgence toward her mother and her family. The second patient harbored unrealistic ideas about having babies and constantly verbalized positive feelings toward the opposite sex.

Compassion, warmth, and empathy must be present in abundance in order to accept and comprehend the first patient's dilemma. An objective appraisal of the second patient's goals must be made. In the face of the biological facts which dictate infertility, medical management should be directed toward long, continued observation of the patient and the encouragement of family members to utilize her capabilities in a satisfying way within the family structure. The satisfaction which she derives from baby-sitting with her sister's children serves to make her feel useful and to offset the futility of being unable to bear her own children. Other similar pursuits may likewise serve to afford her vicarious gratifications. Such a long-range approach to the problem is in keeping with the philosophy of dynamically oriented genetic counseling.[10–13] In this tradition, attempts are made to meet the multifaceted needs of the patient. In the types of problems presented in this paper, the counselor works very closely with the clinical psychiatrist, clinical endocrinologist, and internist.

SUMMARY

Two patients with characteristic phenotypic findings of Turner's syndrome were investigated intensively by an internist-geneticist, a psychiatrist, a social worker, and several psychologists. Chromosome studies of leukocytes confirmed the diagnosis of gonadal dysgenesis in each case. Psychological studies, coupled with psychiatric interviews, showed a differing theme of self-identity in each case. In one of the patients, the concept of her sexual role was completely neutral. In the second patient, there was a slight libidinal drive, and numerous references were made concerning her desire to marry and have babies. It was felt that her responses were influenced by her strong identification with an older sister. The multifaceted medical and emotional problems which were manifested by both of these patients were alleviated through medical-genetic counseling utilizing a team approach.

We wish to express our appreciation to Dr. Aaron Smith for his psychological testing and interpretations of results on these 2 patients and to Arthur L. Larsen, M.D., for his assistance in the cytogenetic studies.

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Neonatal Disorders Affecting Subsequent Neurological and Psychological Development

RICHARD J. SCHAIN, M.D.
Omaha

THE PROBLEMS OF NEONATAL CARE generally have been dominated by efforts to decrease mortality rates during the immediate neonatal period. Considerable success has been achieved in this endeavor through advances in obstetrical and nursery care. However, in recent years concern has been growing over the long-term prospects of infants surviving the neonatal period. This concern is reflected by the interest in development of screening procedures for early detection of inborn errors of metabolism. While this is an important area of investigation, it is also necessary for the clinician to consider the broad spectrum of conditions that affect later development. This paper will review some recently studied neonatal conditions that may adversely affect the developing nervous system. Infectious diseases arising in the neonatal period are relatively well understood and will not be discussed.

Primary defects of the central nervous system due to genetic factors, gross malformations originating during early pregnancy, and the general area of birth injuries will not be considered in this discussion, although at times it may be difficult to distinguish these problems from the conditions to be discussed.

The neonatal conditions discussed here will include: [1] inborn errors of metabolism, [2] disorders of adaptive mechanisms, [3] embryologic defects affecting postnatal brain development, [4] toxic factors, and [5] traumatic factors. Although some of these conditions overlap in the different sections, it has been unavoidable in a classification of this type.

INBORN ERRORS OF METABOLISM

Many of the genetically determined "errors of metabolism" manifesting themselves in childhood are associated with varying degrees of mental retardation.[1,2] In the past, these biochemical defects usually have been detected after appearance of a developmental disorder. At present, however, a growing number of biochemical defects are being detected before the appearance of clinical findings during the neonatal period. Suspicion is often raised by the presence of an affected sibling. The development of dietotherapies that will prevent developmental disorders is a major preoccupation of investigators working in this area.

Phenylketonuria is the best understood inborn error of metabolism associated with mental retardation. It is the one in which there is clear-cut evidence that early dietotherapy mitigates later mental retardation.[3] Routine screening methods for detection of phenylketonuria during the neonatal period are now widely utilized.[4,5]

Many other genetically determined disorders of amino acid metabolism are known to be associated with neurological disease and mental retardation.[6] Maple syrup urine disease, hyperglycinemia, and homocystinuria are examples of disorders of amino acid metabolism that have been detected during the neonatal period.[7–9] Recently, the symptoms of maple syrup urine disease have been controlled with a diet low in the branched-chain amino acids.[10,11] Similar approaches to other amino acid disorders are likely to appear in the future.

Galactosemia is a disorder of carbohydrate metabolism often, but not invariably, associated with mental retardation.[12] Rigid exclusion of lactose and galactose from the diet will reverse the associated symptoms of vomiting, diarrhea, jaundice, and malnutrition. A simple visual screening procedure suitable for use with capillary blood has been developed for the estimation of the deficient enzyme (galactose-1-phosphate uridyl transferase).[13] Galactosemia should be excluded in all neonates with suspicious family histories or clinical symptoms.

RICHARD J. SCHAIN *is research associate professor of neurology, psychiatry, and pediatrics, University of Nebraska College of Medicine, Omaha.*

Nephrogenic diabetes insipidus is a dominant sex-linked disorder of water metabolism primarily affecting males. Vomiting, polyuria, polydipsia, and erratic fever are seen early in life with mental defects frequently occurring later.[14] It has been suggested that early administration of an adequate water intake offers hope for normal development in affected infants.[15] A cautious water deprivation test, with serial measurements of urine specific gravity and osmolarity, establishes the diagnosis.

Pyridoxine dependency is thought to be due to a familial defect in the metabolism of pyridoxine (vitamin B_6) manifesting itself by frequent seizures.[16] This condition has been described in 3 siblings during the first day of life.[17] Administration of 5 to 15 mg. of pyridoxine orally or intramuscularly abolishes the seizure activity. It is wise to give a trial dose of pyridoxine to all neonates with persistent unexplained seizure activity.

DISORDERS OF ADAPTIVE MECHANISMS

A number of biochemical variations occur during the neonatal period that can best be described as failure to adapt to extrauterine life. These are generally considered to be due to inadequate performance of organ or endocrine systems, especially involving hepatic and renal functions. These are not genetically determined disorders, although genetic factors may play a role. They are commonly found in association with conditions affecting fetal or neonatal physiological functions. Consequently, premature birth, maternal disorders such as toxemia or diabetes, and neonatal diseases such as respiratory distress syndrome are frequently associated with these disorders.

Neonatal hypoglycemia is generally considered to be present when the true blood glucose levels are under 20 mg. percent. The hypoglycemia may be asymptomatic or may be associated with tremulousness, lethargy, irritability, cyanosis, feeding difficulties, and convulsions. A recent study has revealed that 50% of the mothers of symptomatic patients had toxemia of pregnancy.[18] Administration of glucose or steroid medication or both improves both the symptoms and the low blood sugar. It appears that neonatal symptomatic hypoglycemia is often associated with later mental and neurological defects, although the causal relationships of these conditions are not clear.[19] However, treatment of symptomatic hypoglycemia seems to be fully warranted by prompt response obtained and the temporary nature of the condition.

Leucine-induced hypoglycemia is a form of hypoglycemia with a strong genetic component.[20,21] Administration of a high protein diet or a leucine load induces hypoglycemic episodes. This condition should be considered in any case of hypoglycemia that persists after the first week or two of life.

The fact that neonates—especially premature infants—often display varying degrees of acidosis has been known for some time.[22] This generally has been considered to be a normal physiological variant of this period. However, severe degrees of acidosis have been shown to be associated with asphyxia neonatorum.[23] Recent experimental work with newborn monkeys indicates that brain damage produced by artificially induced asphyxia can be prevented by administration of alkali and glucose.[24] Studies of premature infants have revealed that prolonged periods of metabolic acidosis (pH 7.10 to 7.25) occur in some infants without associated findings.[25] Information correlating duration and severity of the acidosis with later development is not yet available. However, disturbances in acid-base balance during a critical period of brain development might well exert adverse effects.

Persistently elevated blood phenylalanine and tyrosine levels have been reported in premature infants.[26,27] These need to be distinguished from true phenylketonuria because dietary treatment is not presently indicated for temporary elevations of blood phenylalanine levels without associated increase in phenylketones. It has been suggested that these temporary amino acid imbalances may affect the immature nervous system, but data are not available on this possibility.

EMBRYOLOGIC DEFECTS AFFECTING BRAIN DEVELOPMENT POSTNATALLY

Athyrotic hypothyroidism is the most common variety of hypothyroidism in nonendemic areas. The full-blown mental retardation associated with untreated cretinism is well known but now rarely seen outside institutions for the retarded. More commonly, mild degrees of developmental disorders are found associated with previously treated cases. The importance of rapid, early treatment of hypothyroidism in order to promote maximal intellectual development has been stressed.[28] Ideally, this requires detection of the hypothyroid state during the neonatal period. Constipation, thick skin, large tongue, excessive jaundice, lethargy, and the characteristic facies should raise suspicion of hypothyroidism in the affected infant. Protein-bound iodine or an equivalent determination is the procedure of choice for establishing the diagnosis.

The appearance of hydrocephalus in an otherwise normal infant requires prompt consideration for performance of one of the shunt procedures for hydrocephalus.[29] Considerable divergence of opinion still exists regarding proper indications, but the consensus appears to be that early treatment often improves the ultimate outcome. All cases of suspected hydrocephalus should be transilluminated to help distinguish them from hydranencephaly or other conditions that may simulate hydrocephalus.[30]

Oxycephaly due to premature closure of the cranial sutures may be evident during the neonatal period. X-ray evidence of synostosis of the sutures will confirm the diagnosis. The effect of surgical separation of the sutures on subsequent brain development is uncertain, but the cosmetic effect is clear-cut.

TOXIC FACTORS ARISING IN UTERO OR POSTNATALLY

Hyperbilirubinemia resulting in kernicterus is one of the oldest known causes of brain damage occurring in the neonatal period. It is most commonly due to erythroblastosis fetalis but also can be caused by genetically determined hemolytic anemias or defects in bilirubin conjugation.[31] Premature infants are more susceptible to kernicterus than full-term infants. Kernicterus can be prevented by the use of exchange transfusions at appropriate times. The goal of preventing elevation of blood bilirubin over 20 mg. percent remains a standard rule of thumb in management of this disorder. A number of studies presently under way attempt to correlate elevated serum bilirubin levels per se with subsequent intellectual and neurological development. Final reports have not been published.

Myasthenia gravis may present in the neonatal period as generalized weakness, poor reflex responses, and weak sucking and crying abilities. This picture easily may be attributed to amyotonia congenita or brain damage. The majority of cases are associated with maternal myasthenia resulting in transient neonatal myasthenia.[32] The symptoms, which are apparently due to a curare-like substance passing the placental barrier, disappear after a variable time period of hours to several weeks. True myasthenia gravis also occurs in the neonatal period and requires more prolonged therapy. The diagnosis of myasthenia is primarily established by a favorable response to 1 mg. of edrophonium (Tensilon®). If a positive response is obtained, treatment can be continued with neostigmine (Prostigmin®) or pyridostigmine (Mestinon®).[33]

There has been considerable interest recently in the specific pharmacology of the neonatal period.[34] Sulfonamides and vitamin K in high doses predispose infants to kernicterus. Chloramphenicol is poorly excreted by neonates and may accumulate to toxic levels with weight-adjusted doses that are well tolerated by adults.

TRAUMATIC FACTORS

Subdural hematoma secondary to birth trauma is an important cause of preventable brain damage that is frequently unrecognized in the neonatal period.[35,36] It is especially common when late maternal toxemia has been present. Poor feeding, lethargy, and hypotonia are common, but highly nonspecific, clinical findings. A tense fontanelle is characteristically present. Bilateral subdural punctures through the open anterior fontanelle should be performed on infants with these findings in whom other diagnoses cannot be established. Indications causing the clinician to perform diagnostic lumbar punctures might well be followed by subdural taps. There is some evidence that repeated taps alone might be sufficient treatment of subdural hematoma.[37] However, neurosurgical collaboration should always be obtained if subdural taps are positive.

CONCLUSIONS

The human brain is actively developing during the postnatal period, with especially prominent increases in myelination and axodendritic sprouting.[38] These changes must have implications for later development and are likely to be affected by pathological disturbances arising following entry into extrauterine life. Early detection of such conditions usually cannot rely on conventional neurological diagnosis because the object is to prevent involvement of the nervous system. The increasing number of laboratory procedures available for use during the neonatal period should be freely utilized to establish diagnoses of treatable disorders as early as possible.

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Duplications of the Alimentary Tract

DAVID STEPHENSON, M.D., and
LOYD R. SCHULTZ, M.D.

Omaha

Duplications of the alimentary tract are accessory structures with smooth muscle walls and epithelial linings. They generally are located on the mesenteric aspect of normal intestine. Although they are rare anomalies, they may produce symptoms requiring surgical treatment in the neonatal period or in childhood.

This report is based on patients seen at Childrens Hospital and the University of Nebraska Hospital at Omaha during the past twenty-five years.

EMBRYOLOGY

The embryology of duplications has not been adequately explained. The time-honored theory proposed by Bremer[1] has not proved to be a satisfactory explanation. He suggested that the anomalies arise from incomplete resolution of the solid stage of intestinal development. This theory, however, does not explain duplications that occur in the esophagus or in the colon, since these structures do not lose their lumen and do not show vacuolation.[2]

Sequestration of islands of entodermal cells which have the potential to develop into any type of intestinal or respiratory epithelium is another possible origin that has been proposed.

Environmental changes, such as hypoxia or trauma, occurring in the early fetus are more probable causative factors. Ingalls and Philbook[3] have shown that hypoxia will induce duplications in lower animals, and Louw[4] has presented experimental work to support the suggestion that vascular interference of bowel segments will produce congenital anomalies.

PATHOLOGY

Duplications usually occur as a localized developmental abnormality in the intestinal wall or thoracic cavity. A more complete form sometimes may occur in which the development of the vertebrae, spinal cord, and overlying skin also is involved.

There are two main types of duplications: spherical and tubular. The spherical form seldom communicates with the lumen of the adjacent bowel and is ordinarily lined with mucosa resembling the adjoining segment of gastrointestinal tract. Tubular duplications usually do communicate with the lumen of the adjacent bowel through one or more openings, and at least part of their lining commonly contains gastric mucosa.

Duplications usually lie within the dorsal mesentery of the bowel. They may be intramural and project into the lumen. The muscle coat of the adjacent normal intestine is split and forms a thinned-out covering over the cyst wall. A common blood supply is present between the cyst and the normal bowel. The lining of the cyst is entodermal in origin and usually consists of a single layer of flattened epithelium. This lining may or may not be the same type as the mucosa of the bowel to which the cyst is attached.

SYMPTOMS

The usual symptoms of the spherical abdominal duplication are mechanical, caused by stretching the normal bowel over the mass. This obliterates the lumen and produces partial or total obstruction. Symptoms occur early in fixed segments of the bowel, such as the duodenum or upper jejunum. Lower down the small bowel, duplications may become large enough to be palpable on abdominal examination. Intraluminal duplications may present as the leading point of an intussusception much the same as a polyp would. Symptoms usually develop before 3 years of age, but duplications have been described in adults.[5]

Tubular duplications commonly present with symptoms related to their gastric mucosal lining. Since most of these anomalies communicate with the lumen of the adjacent intestine, peptic ulceration and bleeding may occur at the site of the

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DAVID STEPHENSON *is resident in surgery, University of Nebraska College of Medicine, and* LOYD R. SCHULTZ *is instructor in surgery, University of Nebraska College of Medicine, Omaha.*

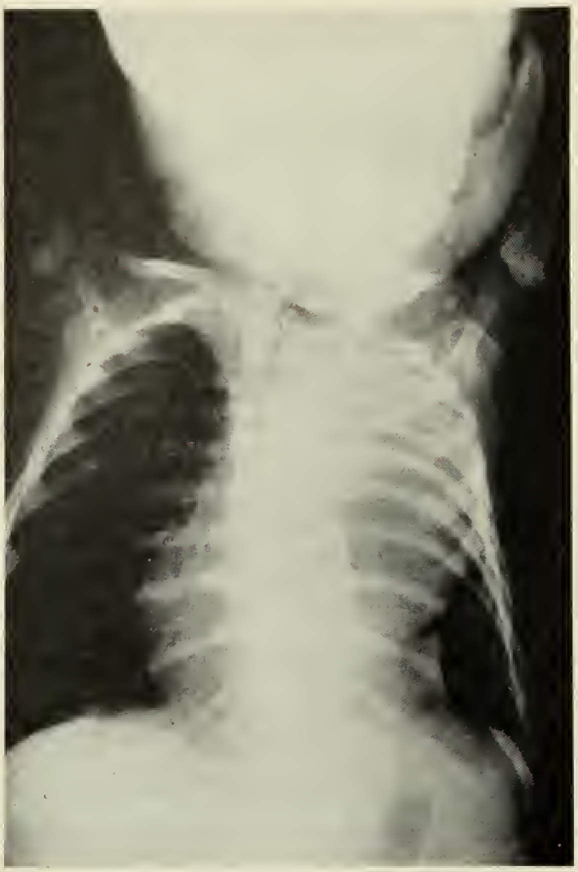

Fig. 1. Case 1. A large cystic esophageal duplication in the left mediastinum, associated with multiple thoracic hemivertebrae

communication or in the duplication itself. This bleeding may be occasional spotting or it may be massive and life threatening. The blood is usually bright red in nature and may be the only symptom of the abnormality. Duplications in the distal small bowel or in the colon more commonly develop ulceration and hemorrhage than those higher in the intestine.[6]

Other manifestations of intra-abdominal duplications have been reported. They include hemorrhagic umbilical discharge through a patent urachal opening[7] and perforation of the accessory structure with peritonitis.[8,9]

The symptoms of esophageal duplications are those of an expanding mediastinal mass. Cough, dyspnea, cyanosis, and recurrent pneumonia are those commonly related to the associated pulmonary and bronchial compression. Dysphagia and vomiting may occur from compression of the esophagus.

Occasionally, distention of the cyst wall causes pain. Pulmonary compression and associated pneumonia have been known to cause repeated hemoptysis.[10]

ESOPHAGEAL DUPLICATION

These anomalies are cystic structures lying in the retropleural region and are often intimately attached to the esophagus. They may appear anywhere from the mouth to the stomach, but the most common site is the middle third of the esophagus.[10]

The following case report includes a fairly typical history and physical findings of these anomalies.

Case 1. This 4-month-old boy was admitted October 23, 1964, with a history of severe raspy cough of two weeks' duration. This was associated with dyspnea and fever. On physical examination, the infant looked undernourished and was pale. Intercostal retraction was present over the left hemithorax. The left lung field was dull to percussion and auscultation. Roentgenographic examination showed a soft tissue density filling three-fourths of the left thorax (Fig. 1). A bronchogram five days later showed bronchial obstruction to the left upper lobe and lingula. Multiple thoracic hemivertebrae added a clue to the diagnosis.

On November 2, a left thoracotomy resulted in removal of a cyst, which had no connection with the esophagus or trachea. The patient recovered uneventfully and was discharged November 10.

PATHOLOGY

Esophageal duplications contain a cyst wall which is thick and is composed of a two-layered muscular wall similar to the esophagus. The mucosa may be either esophageal or gastric (Fig. 2). The contained fluid often resembles gastric juice and produces high titers of hydrochloric acid. There may be peptic ulceration in the cyst wall, with perforation into the pleural space or lung.

Although specific diagnosis is difficult, esophageal duplication should be suggested by symptoms of an expanding posterior mediastinal tumor in an infant. The chest roentgenogram shows a spherical cyst with a homogenous density due to the fluid. There is displacement of the heart and mediastinal structures. Bronchograms show pulmonary compression. The esophagram usually shows esophageal displacement by an adjacent mass, with no fistulous connection between the two.

Vertebral anomalies commonly occur. They were noted in 5 of the 8 esophageal duplications reported by Mellish and Koop.[11] The most characteristic anomaly is a hemivertebra.

A more rare form of duplication that may appear in the chest is one which involves both the chest and the abdominal cavity. These thoracoabdominal duplications are cystic structures which commonly communicate through the retropleural space to the upper small bowel. Occasionally, however, they end blindly in the

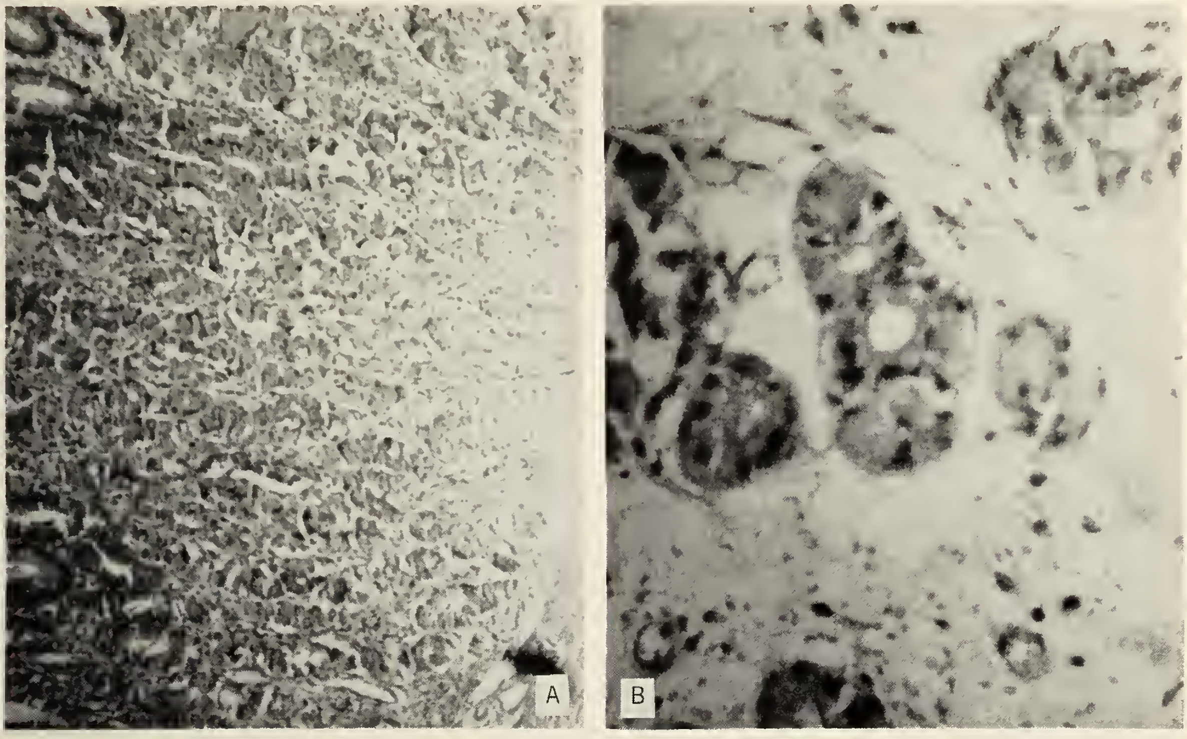

Fig. 2. Case 1. Histologic sections showing the cyst wall of the esophageal duplication. The mucosal lining contains gastric epithelium. [A] × 100, [B] × 430

abdominal cavity. Two cases of esophageal duplications are included in this report. Both were of the spherical, noncommunicating type (see table).

GASTRIC DUPLICATIONS

Duplications of the stomach usually occur along the greater curvature. Because of the good blood supply from the lesser curvature, it is usually possible to excise the accessory structure along with its common stomach wall. There were no cases of gastric duplication in this series.

SMALL BOWEL

Duodenal duplications are rare. These are cystic structures which usually require some form of

SUMMARY OF EIGHT DUPLICATIONS STUDIED

Case	*Age*	*Site of duplication*	*Clinical onset*	*Type of duplication*	*Associated anomalies*
1	14 weeks	Left thorax	Respiratory distress	Spherical, esophageal	Multiple thoracic hemivertebrae
2	12 weeks	Right thorax	Respiratory distress	Spherical, esophageal; gastric lining	None
3	2¾ years	Ileum	Dark rectal bleeding with clots, acute abdominal pain, and perforation with peritonitis	Tubular, with proximal communication into the ileum	None
4	10 days	Ileum	Obstruction and vomiting	Spherical	Malrotation and midgut volvulus
5	4 months	Colon	Diarrhea since birth, palpable mass in left lower quadrant, and bloody stools	Tubular from ileum to sigmoid; proximal communication	Congenital absence, left kidney
6	2 years	Colon	Bright rectal bleeding	Tubular with distal communication; gastric lining	Hirschsprung's disease
7	20 years	Colon	Crampy abdominal pain	Tubular from cecum to descending colon	None
8	6 weeks	Rectum	Mass protruding from anus with straining	Spherical, lined with rectal mucosa	None

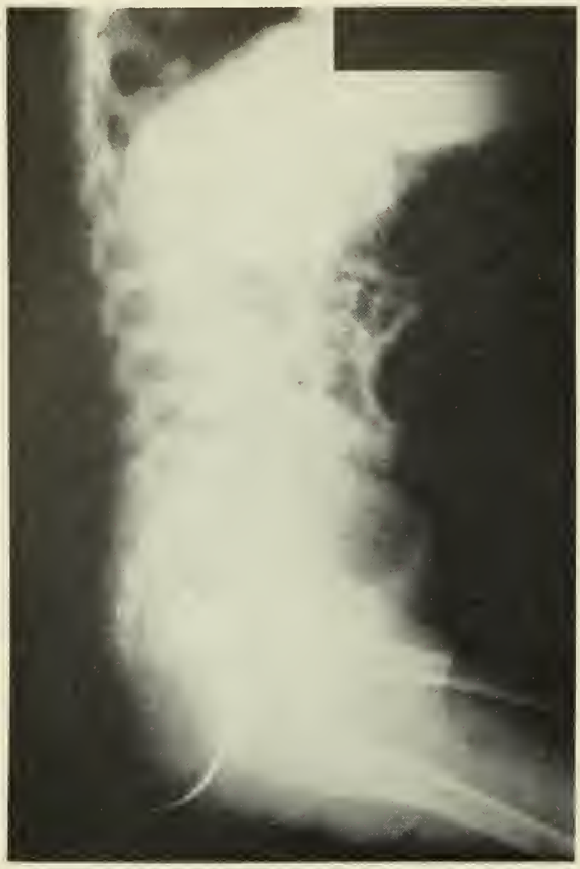

Fig. 3. Case 6. Injection of iodized oil into a rectal duplication which demonstrates its connection into the rectal lumen. The duplication ends as a blind pocket.

internal drainage for decompression. A single limb of jejunum anastomosed to the cyst with a Roux's "Y" anastomosis distal to it has been suggested as a satisfactory method by Bishop and Koop.[12]

Small spherical lesions in the jejunum and ileum usually can be resected along with the adjacent small intestine, and a primary anastomosis is then accomplished. Intramural duplications may be first diagnosed after surgical reduction of a jejunojejunal or ileoileal intussusception.

Barium studies usually do not fill these duplications. However, plain radiographs sometimes show the dilated coils of the abnormality. Vertebral anomalies may occur but are uncommon with abdominal spherical duplication. There were two cases of duplication of the small bowel in this series: one was spherical and the other was tubular (see table).

LARGE BOWEL

Most colonic duplications are of the tubular type. Spherical types do occur in the colon but are more common in the perianal region. Perianal cysts usually do not communicate with the adjacent rectum and present as a gradually enlarging mass close to the anal canal.

Vertebral anomalies of the lower spine have been reported to be frequently associated with tubular duplications.[13] These accessory structures can often be filled with a barium enema because of the associated opening into the colon (Fig. 3). Our series includes four cases of duplication of the large bowel. All were of the tubular type (see table).

A brief summary of Case 6 is presented because of the interesting association of a duplication and Hirschsprung's disease.

Case 6. This 2-year-old boy was admitted February 28, 1964, after having passed three bloody stools in the six hours before admission. The child had been noted to have abdominal distention and recurring fecal impactions since 3 weeks of age. On physical examination the abdomen was soft to palpation. A fecal impaction was felt deep in the left lower quadrant. Laboratory studies were unremarkable.

A barium enema showed a dilated sigmoid colon compatible with Hirschsprung's disease.

Sigmoidoscopic examination showed an orifice in the posterior lateral wall of the rectum on the right side. Mucosal biopsy from this opening was reported to be gastric mucosa (Figs. 4A and B). Rectal muscle biopsy showed no ganglion cells in the bowel wall.

He was discharged and readmitted on April 20. At this time, after injection of iodized oil into the rectal duplication, X-ray demonstrated a cavity 4 cm. in length and 2 cm. in diameter (Fig. 3).

On April 23, a Duhamel-type operation was performed, removing the distal segment of colon and the rectal duplication.

TREATMENT

The surgical treatment of duplications is complete excision of the abnormality, if possible. This is complicated by the location of the lesion in the mesentery of the adjacent bowel. Since the accessory structure shares a common seromuscular layer and blood supply with the normal bowel, inclusion of the involved segment of normal bowel in the resection is necessary.

In cases where there are long segments of bowel involved, this may require resection of enough normal bowel to interfere with normal growth and development. Most tubular colonic duplications are of this type.

Marsupialization into adjacent normal bowel has been used in these cases and in those in which resection is hazardous because of the location. Gastrointestinal bleeding with peptic activity from retained gastric mucosa is always a hazard when marsupialization is used. Wrenn[14] recently described a technique of stripping the mucosal lining from the duplication through multiple transverse incisions in the seromuscular layers of the duplication. In this way, the es-

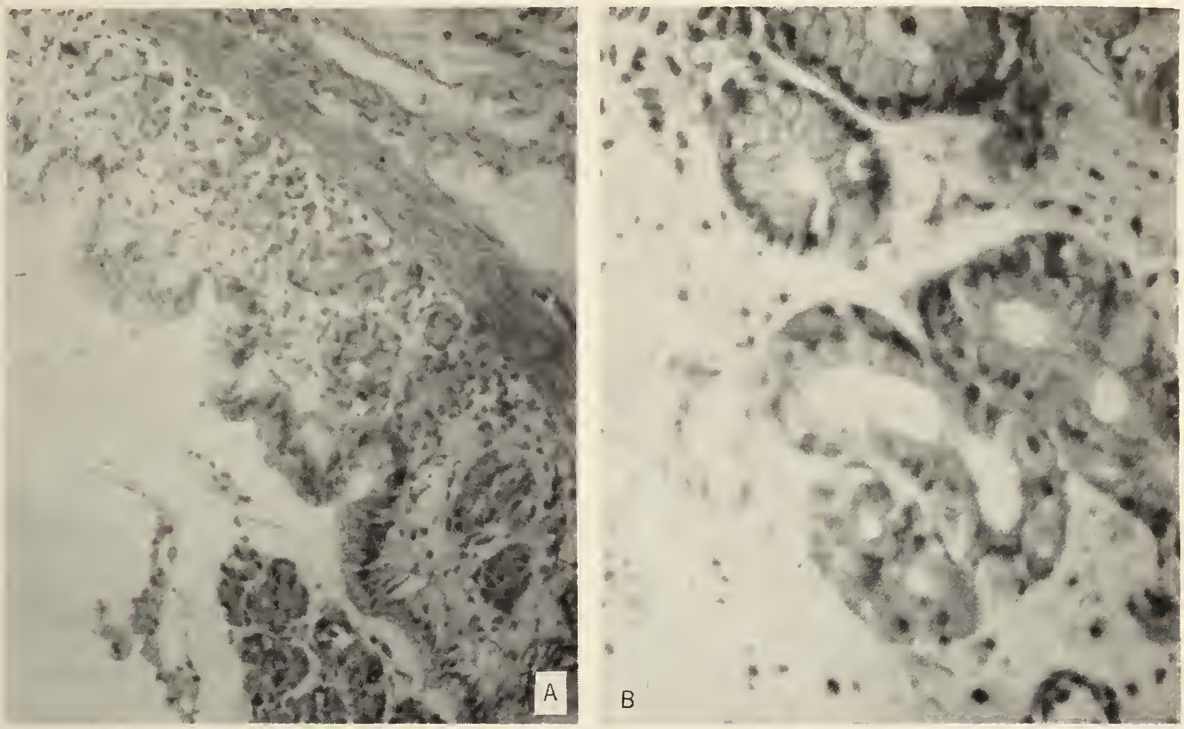

Fig. 4. Case 6. Photomicrograph of rectal duplication. The mucosal lining contains gastric mucosa. [A] × 100, [B] × 430

sential blood supply of adjacent normal intestine is preserved, and yet the gastric mucosal lining in the accessory bowel is removed. An alternative method of treating these long tubular duplications is to resect the distal end of the duplication and adjacent bowel. Internal drainage is then reestablished by cutting back the common bowel wall for a short distance. The stoma is then anastomosed to the single lumen distally.

Esophageal duplications may present a special problem in the surgical treatment. These cysts sometimes share a common muscularis with the esophagus in as much as two-thirds of its length.[10] Under these circumstances, an attempt to excise the cyst may result in an extensive esophageal wall defect. Because of the nature of this attachment, decompression of the cyst by marsupialization, with subsequent destruction of the mucosal lining by packing and curettage, has been recommended.[10]

Abdominal extension of a duplication from the thorax may not be discovered until mobilization at thoracotomy. In these cases, closure of the tract at the diaphram has been suggested.[12] A second procedure through the abdomen is then undertaken later, and a lengthy double operation is avoided.

DISCUSSION

Duplications of the bowel can be classified into 2 anatomical types: spherical and tubular. The spherical type does not usually retain a connection with the associated segment of normal intestine, while the tubular duplication does. Gastric lining is commonly found in the tubular as well as the spherical esophageal type. Other spherical duplications are usually lined with intestinal mucosa similar to that of the small bowel or colon.

The presenting symptoms are related to the location of the duplication and to the type of lining in the cyst wall. Since most tubular duplications secrete gastric juices and are connected with the bowel lumen, bleeding from peptic ulceration is common. Three of the four tubular duplications in this group of patients had rectal bleeding. The other presented with a perforation of the accessory structure.

The spherical duplications of the esophagus produce symptoms of an expanding intrathoracic mass. Respiratory distress was the presenting symptom in both of our children with esophageal duplication.

The ileum was noted to be the most common site of origin in a series of 38 duplications reported by Mellish.[11] The colon and rectum were the most common sites of origin in this study.

Other congenital anomalies are commonly associated with these abnormalities. Of the 8 cases in this series, one had hemivertebrae, one had Hirschsprung's disease, one had malrotation of the midgut, and one was without a left kidney.

All 8 patients had surgical procedures, and one died due to an associated complication of volvulus with midgut malrotation.

CONCLUSION

Eight cases of duplication of the alimentary tract have been presented. These anomalies may occur at any site from the mouth to anus. Although etiology is unknown, it is probably due to early fetal distress or vascular obstruction.

Tubular duplications usually have an opening into the associated bowel and commonly contain gastric mucosa. Spherical duplications seldom retain a communication with the bowel.

Respiratory distress is the most common presenting symptom of those in the thoracic cavity. Rectal bleeding or perforation is the most frequent presenting symptom of the tubular form, and obstructive symptoms are commonly associated with the spherical type.

Surgical treatment depends on the location and the type of anomaly. Resection is the treatment of choice, but this may be impossible without removing large segments of normal bowel because of the common muscular wall between the two. In these cases, marsupialization or stripping of the mucosal lining of the duplication is suggested. Long tubular duplications may be treated by cutting back the common muscular wall and forming a single stoma anastomosis distally.

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Acute Renal Failure in Childhood

CAROL R. ANGLE, M.D.
Omaha

ACUTE RENAL FAILURE, a formidable event at any age, is possibly more often reversible in the child than the adult. Early recognition of impending or existent renal failure, etiologic diagnosis, and vigorously conservative management are all essential to salvage of those children with reversible insufficiency. This outline of the management of acute renal failure includes a brief review of the pathology, etiology, and diagnostic criteria.

The value of a clinical diagnosis of a prerenal, renal, or postrenal etiology has been stressed by Merrill.[1] Prerenal implies a functional insufficiency secondary to circulatory changes and postrenal, an obstructive uropathy. It is important to recognize these functional responses since they both are readily reversible, but if sustained, they produce parenchymal damage which heals only by slow regeneration. Parenchymal damage may be secondary to prerenal or postrenal changes as well as to a variety of glomerular and tubular reactions (Table 1), acute glomerulonephritis being the most common in childhood. Taking all ages into consideration, acute tubular necrosis is the most common morphologic change associated with acute renal failure and the two terms are used synonymously.[2]

Oliver,[3] in his classical microdissections, differentiated the relative destruction in acute tubular necrosis due to ischemia and due to nephrotoxins. Ischemia produces functional renal insufficiency followed by tubulorrhexis which occurs randomly along a nephron, not, as previously thought, only in the distal or "lower" nephron. There is complete disruption of tubular continuity and of the basement membrane. Healing of the lesion occurs by regeneration of epithelial cells only in areas with an intact basement membrane and is therefore erratic. The nephrotoxins produce a uniform necrosis down to, but not including, the basement membrane so that regeneration is uniform, but Oliver pointed out that lesions typical of ischemia may also occur.

Other authors[4,5] have described associated glomerular involvement ranging from hyalinization of the glomeruli to periglomerular fibrosis in biopsies[4] done long after recovery. Residual tubular changes are atrophy and interstitial fibrosis in a patchy distribution. Any decrease in blood supply through the glomeruli will involve the tubules, but even total disruption of affected nephrons is compatible with recovery in the less involved nephrons.

Considering the frequency of extreme dehydration in infants, acute tubular necrosis is a rare event. Acute tubular necrosis in children may be a sequel of circulatory insufficiency such as dehydration, shock, surgery, burns, sepsis, and, commonly, nephrotoxins. Two of the five deaths due to accidental poisoning in children reported to the Nebraska Master Poison Control Center in the years 1957 to 1964 have had acute renal failure: aspirin, a very rare cause of renal failure, in one child and a combination of methyl alcohol, arsenicals, and mercury salts in the other.

These are some of the currently important nephrotoxins, taken from an extremely long list.[1,6]

- Aminopyrine[7]
- Arsenic
- Bacitracin
- Bismuth
- Cadmium
- Carbon tetrachloride and other chlorinated hydrocarbons
- Disodium calcium edetate
- (Di) Ethylene glycols
- Fluorides
- Gold
- Lead
- Mephenesin
- Mercury compounds
- Neomycin
- Phenacetin
- Phenol
- Phenurone
- Phosphorus
- Polymyxin
- Potassium chlorate
- Quinine
- Sulfonamides
- Tetracycline, degraded
- Turpentine
- Uranium

In thrombosis of the afferent arteriole, the glomerulus becomes infarcted and destroyed and so does the entire nephron. If the vascular lesion is severe, all the cortical glomeruli are infarcted, and the almost always fatal syndrome is termed symmetrical cortical necrosis. Only ten survivors from bilateral renal cortical necrosis have been

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CAROL R. ANGLE *is assistant professor of pediatrics, University of Nebraska and Creighton University, Omaha.*

TABLE 1

CAUSES OF ACUTE RENAL FAILURE IN CHILDREN

- Circulatory:
  - Dehydration
  - Sepsis
  - Shock: surgery, trauma, and burns
  - Renal vein thrombosis
  - Renal artery occlusion
- Parenchymal:
  - Acute glomerulonephritis: poststreptococcal and membranous nephritis (nephrotic syndrome)
  - Renal vasculitis: hemolytic-uremic syndrome, anaphylactoid purpura, lupus, polyarteritis, and sickle-cell crisis
  - Nephrotoxins: metals, chlorinated hydrocarbons, glycols, and so on
  - Precipitins: calcium, oxalates, uric acid, myoglobin, and hemoglobin
- Obstructive uropathy:
  - Congenital
  - Neurogenic
  - Precipitins: uric acid and sulfadiazine

described in the medical literature.[8] Renal cortical necrosis has been reported in infancy and childhood, most often with the dehydration of vomiting and diarrhea,[9] severe infections,[10] transfusion reaction,[11] and shock from multiple causes including traumatic delivery.[12]

Parenchymal disease characterized by a diffuse vasculitis is also a form of ischemia; this includes the hemolytic-uremic syndrome, anaphylactoid purpura, lupus, polyarteritis, sickle-cell crisis, and bacterial endocarditis. The hemolytic-uremic syndrome of infancy, in which the anuria may be reversible, has a variable pathology, but the chief finding is vascular occlusion.[13,14] Bilateral renal cortical necrosis due to fibrinoid necrosis of medium-sized arteries, vascular thrombotic lesions resembling thrombotic thrombocytopenic purpura, and a nephritis consisting of scattered glomerular lesions characterized by hyaline thrombosis and occlusion of capillary loops have all been described. The pattern of nephron destruction in this last group of patients[14] has not been clearly related to the glomerular lesions, but microdissections have not been done. In a very simplified view, ischemia sequentially produces functional changes first followed by tubular destruction; this ischemia may be associated with or due to visible arteriolar or arterial obstruction.

Other causes of acute, potentially reversible renal pathology are a function of renal ischemia only in the broadest sense. Tubular precipitins such as uric acid in infants or in leukemic children treated with cytolytic agents, calcium in hyperparathyroidism or acute vitamin D intoxication, hemoglobin, and myoglobin are more reasonably called direct causes of nephropathy.

Obstructive lesions of the urinary tract may be the major cause of the unusual phenomenon of absolute anuria.[1] Experimental data, reviewed by Thurau,[15] suggests that elevation of intratubular pressure increases the resistance to postglomerular capillary blood flow with the resultant tubular ischemia a factor in the nephron destruction of acute obstructive nephropathy. Increased intraluminal pressure is also associated with a decrease in blood flow through the vasa recta of the inner medulla, possibly contributing to the preferential destruction of the renal papillae.[16]

Acute renal failure in childhood is most commonly a phase of acute or chronic nephritis:[17] poststreptococcal, anaphylactoid purpura, or membranous nephritis (nephrotic syndrome). Even if chronic nephritis is known to preexist, a biopsy showing functioning glomeruli will be an indication for careful management of the acute stage with the possibility of recovery to a compensated state of chronic nephritis. Estimation of the possibility of recovery is essential since, at the present time, no one advocates long-term dialysis programs for the management of the child with chronic nephritis.[18] Kidney transplants in children are more feasible, and careful management of the acute renal decompensation may allow for transportation and evaluation of the child. Some of the many causes of acute renal failure, most of which have the possibility of partial or complete recovery, are outlined in Table 1.

DIAGNOSIS

The exclusion of compensatory oliguria due to dehydration and the distinction between functional and morphologic renal failure are of critical importance in the oliguric patient with dehydration or circulatory insufficiency. Prompt rehydration and restoration of cardiac output are imperative in all three, especially since each stage leads to progressive renal ischemia. Acute renal failure may be distinguished from the oliguria and azotemia of dehydration by the following criteria.

Urine volume $<$ 275 ml. per square meter of body surface per day[19]

Urea $\frac{\text{urine}}{\text{plasma}} < 14$[20,21]

Urine urea $<$ 1100 mg. percent in presence oliguria[22]

Infants with severe dehydration and oliguria but without renal failure usually have a blood

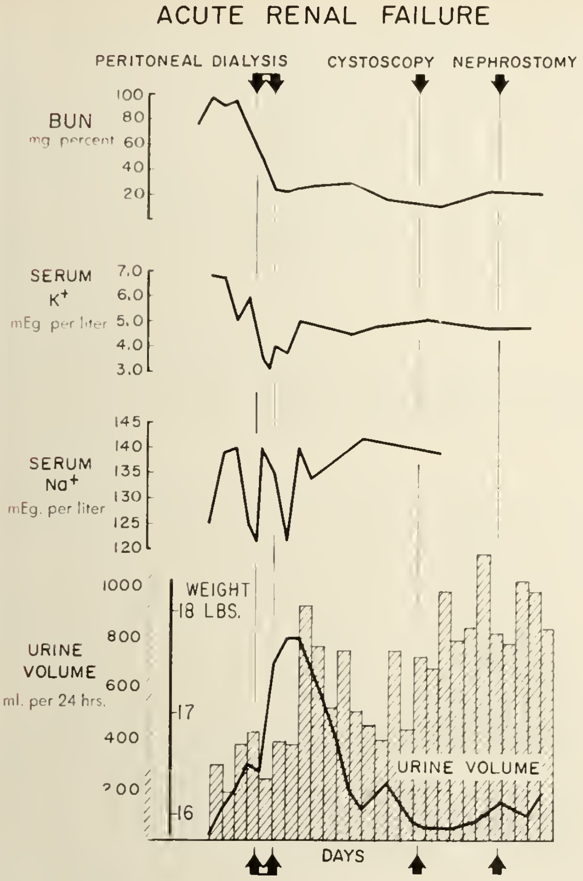

Fig. 1. Single peritoneal dialysis of twenty-eight hours for acute renal failure, precipitated by pneumococcal meningitis, in a 7-month-old boy with previously undiagnosed bilateral hydronephrosis and pyelonephritis. Diuresis occurred within four days of the dialysis.

urea nitrogen (BUN) of 80 to 120 mg. percent. Unlike the values in the child with renal failure, the urine urea is 10 to 20 times the blood urea, and adequate hydration, often including whole blood, is associated with increased urine volume and gradual decline in the BUN.

Once the patient is hydrated, a test dose of 15 or 20% mannitol, 0.2 gm. per kilogram given rapidly intravenously, is very useful to distinguish functional renal failure from acute tubular necrosis.[20,21] In the former, there should be a 50% increase in urine volume in the two hours following the mannitol, this being the indication for sustained hydration and osmotic diuresis with additional mannitol. Luke and associates[20] suggest repeating the trial dose of 20% mannitol before embarking on the conservative regimen for acute renal failure.

These stringent criteria, including failure to respond to mannitol, have been established for acute tubular necrosis in order to refine the diagnosis and evaluate the therapy.[2] Not all of these criteria are essential to the diagnosis of acute severe renal insufficiency that will benefit from conservative management and, possibly, dialysis, as illustrated by the following case.

CASE REPORT

This 7½-month-old boy (CMH No. 59652) was admitted because of convulsions with fever and irritability for two days. Past history was unremarkable except that he had always had "stop-go" micturition. He was acutely dehydrated and comatose and had a distended abdomen. Initial spinal fluid was clear but Diplococcus pneumoniae were recovered on culture and subsequent cerebrospinal fluid (CSF) specimens were consistent with the diagnosis of meningitis. Triple therapy with penicillin, streptomycin, and chloramphenicol was started on admission along with rehydration. The changes in body weight, urine volume, and blood chemistries are shown in Figure 1.

His hydration improved but urine osmolality was only 243 mosm. per liter, despite a low volume and a serum osmolality of 293 mosm. per liter. Urine specific gravities were all below 1.010. The BUN did not decline appreciably. Urine urea was 290 mg. percent on the third day of therapy with $\frac{\text{urine urea}}{\text{blood urea}} = 4.1$. Serum potassium decreased to 5.9 mEq. per liter on the third day but the electrocardiogram showed marked peaking of the T waves. The bladder was distended and drained by indwelling catheter with a presumptive diagnosis of congenital obstruction of the bladder neck. Because of his very poor clinical condition, in addition to the laboratory findings, a peritoneal dialysis was carried out for twenty-eight hours on the fourth day of hospitalization.

As shown in Figure 1, there was rapid correction of the serum chemistries. He did retain fluid from the dialysis for four days, at which time there was a brisk diuresis and associated correction of the hyponatremia. His general condition improved rapidly after the single peritoneal dialysis and urologic evaluation and nephrostomies were well tolerated.

This baby did not fulfill all of the criteria of acute renal failure since his urine volume was in excess of 275 ml. per square meter of body surface per day, but he did have symptomatic renal insufficiency and his clinical status improved markedly with peritoneal dialysis. Infants with congenital urinary obstructions and azotemia may be so critically compensated that they are unable to withstand surgery, rapid urinary decompression, or sepsis and, in such babies, peritoneal dialysis is invaluable.

MANAGEMENT OF ACUTE RENAL FAILURE

Fluids and electrolytes. Oliguric phase. The dehydrated patient should be rapidly and appropriately hydrated by the usual parameters. We employ 2,500 ml. per square meter of body surface per day, or 30 ml. per kilogram per day in addition to maintenance fluids, if moderately dehydrated, and 3,500 ml. per square meter of

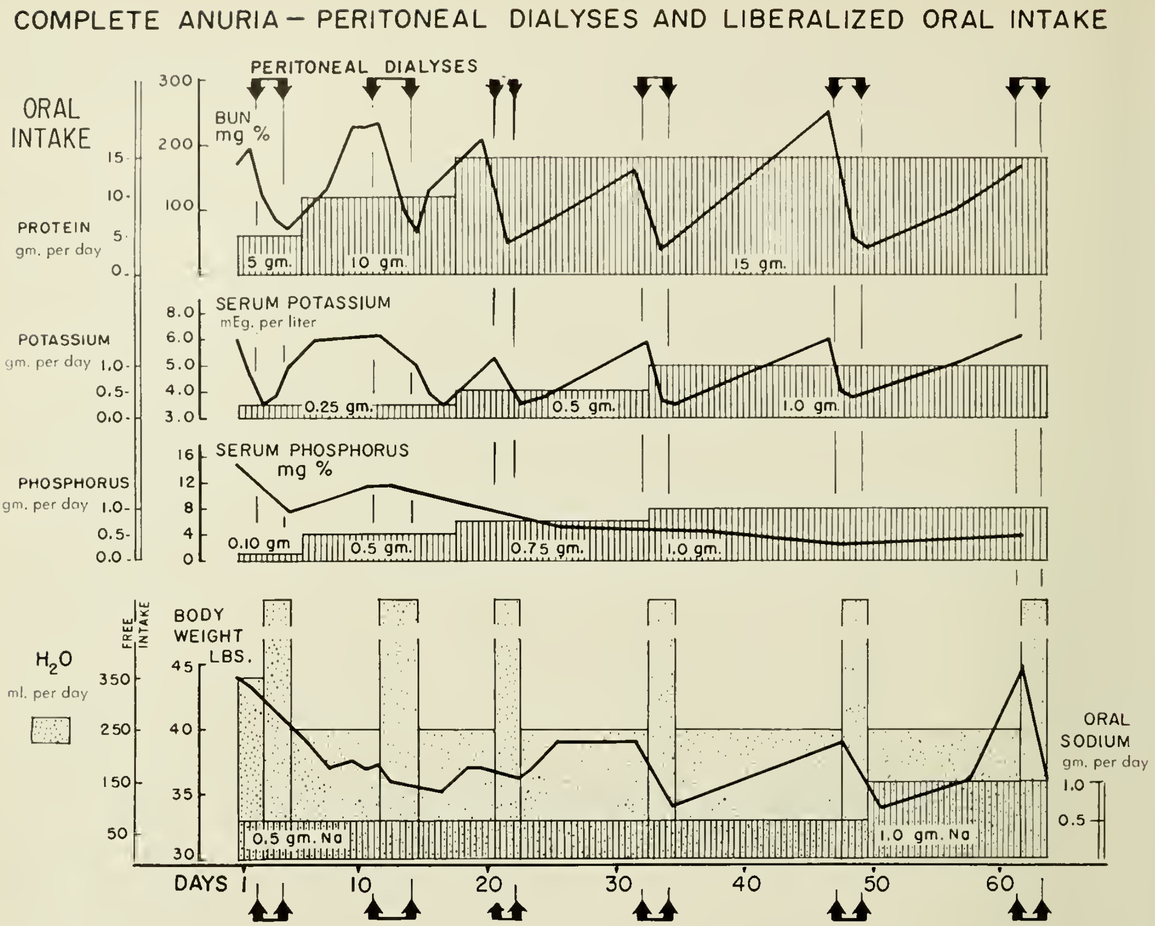

Fig. 2. 5½-year-old girl, 0.68 M², with membranous nephritis who was anuric except for three days' output of less than 25 ml. per day. Note the weight gain on an oral intake of 400 ml. per square meter of body surface per day. The increased allowances of protein, phosphorus, and potassium had no effect on the rise of the serum levels between dialyses. This stabilization is typical of chronic renal failure.

body surface per day, or 60 ml. per kilogram per day in addition to maintenance fluids, if severely dehydrated. Shock should be treated with dextran, fresh frozen plasma, or blood as indicated. As in all dehydrated patients, potassium is never given until the urinary status is evaluated, but this does not eliminate the use of blood if it is essential. Since renal acidosis is anticipated and if alkalosis has been ruled out, at least one-half of the anion is given as lactate or bicarbonate rather than chloride.

The edematous child with acute renal failure should be given the absolute minimum amount of fluid required to administer other substances such as carbohydrate, calcium gluconate, or sodium bicarbonate. In acute glomerulonephritis with oliguria, for example, many children are given only hard candy and small amounts of Karo-sweetened ginger ale for the first few days. Vomiting is not an indication for intravenous fluid if the child is edematous.

The adequately hydrated child is maintained on 250 ml. per square meter of body surface per day plus fluids equal to the previous day's urinary output. Accurate daily weights are obtained and a daily loss of about 0.5 to 1% of body weight is considered appropriate. Figure 2 shows the weight changes in a 5½-year-old girl (CMH No. 20,197) with acute anuria in the course of chronic membranous nephritis. There was a moderate weight gain on an intake of 400 ml. per square meter of body surface per day. This larger amount was given since restriction to 250 ml. per square meter per body surface per day (170 ml. per 0.68 square meter of body surface, including preformed water in her food) was intolerable.

Fluid and electrolyte administration in the oliguric phase is very restricted unless dehydration and other acute deficits are present. An outline of therapy, similar to that employed by others,[1,19,23] is given in Table 2. Carbohydrate,

TABLE 2

FLUID AND ELECTROLYTES IN OLIGURIC PHASE OF RENAL FAILURE

	Acute	*Subacute (oral)*
Fluid	250 ml. per square meter of body surface per day + urinary loss	250 ml. per square meter of body surface per day + urinary loss
Dehydration	As needed	
Edema	Minimum to administer carbohydrate and $NaHCO_3$	
Carbohydrate	60 gm. per square meter of body surface per day (minimum)	Increase as tolerated. Add as much fat as tolerated to at least 1,500 calories per square meter of body surface per day.
Protein	0	15 gm. per square meter of body surface per day (on demand)
Sodium	2 to 3 mEq. per kilogram of molar Na lactate or molar $NaHCO_3$ for hyperkalemia or acidosis	0.5 to 0.75 gm. per square meter of body surface per day on demand or as needed for hyperkalemia or acidosis
Potassium	0	1 gm. per square meter of body surface per day (on demand)
Calcium	10% calcium (Ca) gluconate, 1 ml. per kilogram, intravenously, as necessary	Ca gluconate, 1.25 to 4 gm. before each meal
Phosphorus	0	1.5 gm. per square meter of body surface per day (on demand) with aluminum carbonate gel after meals

in a minimum amount of 60 gm. per square meter per body surface per day (1.5 to 2 gm. per kilogram per day) has a protein-sparing effect and may be given intravenously for a few days as 10 to 20% solutions or by gavage tube as a 50% solution. After vomiting subsides, children rapidly tire of the initial diet of hard candy and Karo-sweetened ginger ale. "Butter balls" are universally refused. The dietitian, following the child's food likes, can usually plan an acceptable diet around unlimited fat and carbohydrate, with the allowance of 15 gm. per square meter of body surface per day of protein, 1.5 gm. per square meter of body surface per day of phosphorus, 1 gm. per square meter of body surface per day of potassium, and 0.5 to 0.75 gm. per square meter of body surface of sodium. Such a diet makes it possible to achieve a minimum caloric intake of 1,500 calories per square meter of body surface per day.

McCracken and associates[24] have demonstrated that 20 gm. of protein (3 eggs) can be given adults with chronic renal failure without an appreciable increase in urea production. In Figure 2 is shown the tolerance of a protein intake increased from 5 gm. (0.33 gm. per kilogram) to 15 gm. (1 gm. per kilogram) in this 5½-year-old girl with complete anuria. No protein is given in the acute phase, but in the subacute or early chronic phase, the actively complaining and hungry child may be allowed 15 gm. per square meter of body surface per day (0.3 gm. per kilogram). In chronic renal failure, the Giordano-Giovanetti[25] diet of about 10 to 12 gm. of protein per square meter of body surface per day has been shown by Berlyne and Shaw to be associated with terminal agitation and bleeding but with none of the usual gastrointestinal symptoms.[26]

Anabolic steroids such as norethandrolone (Nilevar®) are often used in adults to minimize protein catabolism; their use is limited in the child by the fact that virilization may appear within one week.

The tolerance for variable allowances of potassium, phosphorus, and sodium are also shown in Figure 2. In the period charted, this girl was totally anuric with the exception of three days with a urine output of less than 20 ml. per day. She had mild diarrhea throughout, and this probably contributed to her tolerance for an increase in potassium from 250 mg. to 1 gm. per day. Since it is difficult to devise a low-phosphorus diet, she was allowed 1 gm. per day. With administration of 30 cc. of aluminum carbonate gel after each meal, she developed hypophosphatemia, and the dietary phosphorus could again be increased.

Symptomatic hyperkalemia may be forestalled by complete restriction of potassium and by adequate carbohydrate to minimize protein catabolism. A resin, sodium polystyrene sulfonate (Kayexalate®), is useful in a dose of 1 to 2 gm. per kilogram per day, given as 2 or 3 enemas of the 10% suspension. In acute hyperkalemia with electrocardiographic changes, molar sodium bicarbonate ($NaHCO_3$) or molar sodium (Na) lactate,[2,3] 2 to 3 mEq. per kilogram, given slowly intravenously, with electrocardiographic monitoring, may be highly effective as shown in Figure 3. This 6-year-old boy had acute glomerulonephritis with severe oliguria and when first seen, on the sixth day of his illness, BUN was 186 mg. percent and serum potassium 9.4 mEq. per liter. It is rare to see oliguria persisting beyond the fifth day in poststreptococcal glomerulonephritis and diuresis was anticipated. On the seventh day, serum potassium was 9.9 mEq. per liter and BUN 201 mg. percent. The electrocardiogram showed tall peaked T waves with an idioventricular rhythm. Reversal of these extreme findings is shown during the administration of 40 ml. of molar sodium lactate (2 mEq. per kilogram). In this boy, hemodialysis was carried out the same day. After the acute phase, he never made a complete recovery and, one year later, had chronic glomerulonephritis with anemia, azotemia, and hyperkalemia.

Gastrointestinal symptoms. Nausea and vomiting may be controlled with phenothiazine derivatives such as suppositories of trimethobenzamide HCl (Tigan®). Persistent vomiting is one of the indications for dialysis. Diarrhea or paralytic ileus may occur. Diffuse hemorrhagic gastritis and bleeding from small gastric or duodenal ulcers are common and are treated symptomatically as well as improving with dialysis.

Cardiovascular symptoms. Hypertension is initially treated with 0.07 mg. per kilogram of intramuscular reserpine, repeated in twelve to twenty-four hours, if necessary, followed by a maintenance dose of 0.01 mg. per kilogram every eight hours.[27] Hydralazine, 0.10 mg. per kilogram, is added if the child has encephalopathy or cardiac failure or if blood pressure does not decrease with reserpine. The addition of guanethedine (Ismelin®), beginning with 10 mg. per day and increasing to as high as 50 mg. per day, is helpful in severe, refractory hypertension. Since Ismelin® produces an orthostatic hypotension, control of the diastolic pressure when sitting but not necessarily when supine is adequate.

Digitalization for cardiac failure may precipitate ventricular arrythmias, and for this reason, single dose, intravenous digitalization should be avoided.[1]

Hyponatremia, hypercalcemia, and acidosis all mimic or accentuate the electrocardiographic changes attributed to hyperkalemia. The pacemaker shifts downward producing, successively, wandering pacemaker, nodal, and then idioventricular rhythm. The T waves become narrow and peaked with shortening or the QT interval. Due to intraventricular block, QRS is prolonged.

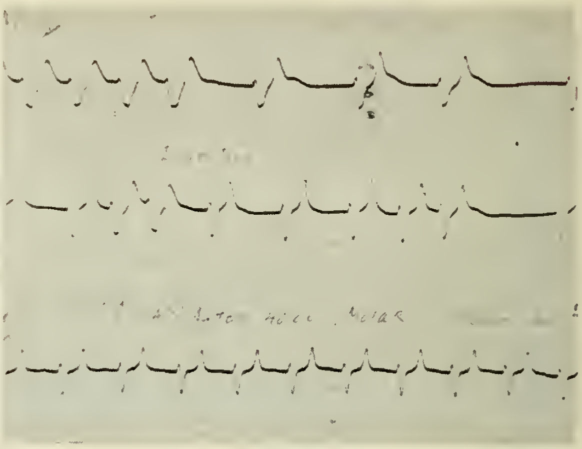

Fig. 3. Top: idioventricular rhythm of extreme hyperkalemia (9.9 mEq. per liter). Middle: during intravenous injection of molar sodium lactate, 2 mEq. per kilogram. Bottom: completion of injection. All Lead I.

Fibrinous pericarditis is relatively frequent in acute renal failure but is compatible with recovery and should not be accepted as a terminal event.

Central nervous system manifestations. In addition to hypertensive encephalopathy and hypocalcemic tetany, there are many poorly explained derangements of the central nervous system. These vary from lethargy and coma to the more common hyperirritability, hyperreflexia, and twitching. The child may be disoriented and agitated. Phenobarbital should never be used for sedation, since it is normally excreted only in the urine, but paraldehyde, short-acting barbiturates, diphenylhydantoin (Dilantin®), and phenothiazines may be used as sedatives or anticonvulsants.

Hematologic disorders. Bleeding diatheses are distressingly frequent in renal failure and have recently been reviewed by Leiken.[28] They may be due to a decrease in platelets or platelet function with poor thromboplastic generation corrected by normal platelets. Coagulation defects have been attributed to decreases in factor II (prothrombin), factor V (proconvertin), factor VII (proaccelerin) and factor IX (plasma thromboplastin component or PTC) activity. If the general defect can be ascertained, therapy would include platelet transfusions and possibly steroids for the first group and vitamin K and fresh-frozen plasma for the coagulation deficits.

Anemia is the rule, and transfusion with fresh, whole blood or packed, red cells is recommended if the hematocrit falls below 25 or if there are other indications such as chronic bleeding, severe infection, or a surgical procedure.

Infection. Bacterial infection, especially lobar pneumonia, pyonephrosis, and wound infection, is the direct cause of death in our own patients more often than the biochemical derangements. Environmental asepsis is important, especially in patients with peritoneal dialysis. The risks of the indwelling urinary catheter cannot be emphasized too often; if a catheter is absolutely essential to patient management, frequent irrigation, catheter changes, urine cultures, and appropriate therapy are required. Prophylactic antibiotics are of no value since infection with a resistant organism is the immediate sequel.

Antibiotics that depend mainly on renal elimination must be given in reduced dosage, and the renal damage of bacitracin, neomycin, kanamycin, and the polymyxins may accentuate the renal pathology. An outline of recommended chemotherapy in renal insufficiency is as follows:[29,30] [1] usual to slightly reduced dose—penicillin, methicillin, oxycillin, erythromycin, chlortetracycline, novobiocin, and cephalothin (chloramphenicol, only with blood levels), [2] reduced dose—tetracycline, demethyltetracycline, oxytetracycline, ampicillin, neomycin, kanamycin, polymyxin B, colymycin, and vancomycin, [3] with extreme caution only—streptomycin, bacitracin, ristocetin, nitrofurantoin, and sulfas, and [4] dialysible[31]—streptomycin, penicillin, tetracycline, sulfonamides, chloramphenicol, nitrofurantoin, and isoniazide.

Peritoneal dialysis. Peritoneal dialysis is a simple, safe, and widely used method of carrying infants and children through acute renal failure.[1,13,14,27,31,32] Hemodialysis is more efficient and the only feasible technique in situations such as burns and abdominal surgery, but it is not universally available and must be carefully controlled for small infants.[33] In severe uremia, the very rapid decline in blood urea achieved by the artificial kidney may be deleterious because of the blood-brain urea ratio with hyperosmolality of the spinal fluid.[13]

Indications for peritoneal dialysis in the child with acute renal failure include progressive azotemia, hyperkalemia, acidosis, edema and hypervolemia, severe vomiting or central nervous system (CNS) symptoms, and cardiac failure.[27] The procedure as outlined in the product brochures accompanying the commercial sets (Abbott, Baxter) is adequate, but the refinements described by Barry and Schwartz[32] are most helpful. The role of a single peritoneal dialysis in tiding a young infant through an episode of meningitis and renal insufficiency is shown in Figure 2.

Diuresis. In acute tubular necrosis, diuresis may occur as late as thirty-one days after the onset of oliguria, the duration of oliguria being unrelated to the prognosis.[2] After recovery from acute tubular necrosis, there is a mild, permanent diminution of renal function, but prognosis is relatively good in the younger patient.[4,5,17,34]

In the oliguria of acute poststreptococcal glomerulonephritis, diuresis almost always occurs by the seventh day and usually by the fifth day of oliguria. Protracted oliguria in acute glomerulonephritis, anaphylactoid purpura, hemolytic uremic syndrome, and other renal disease is an indication for biopsy to determine the prognosis for recovery; the absence of functional glomeruli in an adequate biopsy specimen is a contraindication, at present, to continued dialyses.[35]

Diuresis usually begins with at least a fifty percent increase in urine volume with a greater volume on the second day. Early, the urine sodium may be around 100 mEq. per liter and urine potassium about 30 mEq. per liter,[22] but by the seventh to tenth day, sodium usually can be reabsorbed at 20 mEq. per liter.[36] Measurements of urine concentration are highly desirable, but since there is usually an accumulation of water and electrolytes, not all of the loss is replaced in the first few days. Water and salt loss is less of a problem in the early recovery phase of acute glomerular nephritis than of acute tubular necrosis.

SUMMARY

Acute functional renal failure can be distinguished from that due to morphologic changes by the response to hydration and mannitol, and this distinction should be made promptly. In children, glomerulonephritis and glomerular vasculitis are more frequent causes of acute renal failure than acute tubular necrosis. The importance of nephrotoxins in acute tubular necrosis of childhood should not be underestimated. The management of acute renal failure in childhood is reviewed since recovery, related to etiology, is more likely in the child than the adult.

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Evaluation of a Poison Information Center

CAROL R. ANGLE, M.D., and MATILDA S. McINTIRE, M.D.

Omaha

THE NEBRASKA Master Poison Control Treatment and Information Center at Childrens Memorial Hospital, Omaha, began operation in 1957, just after the establishment of the National Clearinghouse for Poison Information Centers of the United States Public Health Service and the American Association of Poison Control Centers. In duration of activities, the number of patients treated and total reported cases, the center is in the median group of the 341 that report accidental poisonings to the National Clearinghouse.[1]

During its seven years of operation, 600 to 800 children have been treated annually and 100 to 300 telephone reports of accidental ingestion of toxic substances are filed with the National Clearinghouse for Poison Control Centers. Total calls to the center were 3,028 in 1964, but only 204 were reported[1] since the majority did not involve reportable ingestions of toxic substances.

Evaluation of the center, which provides twenty-four-hour telephone information service for physicians and parents in addition to treatment facilities, was prompted by (1) the drain of calls upon the time of a resident who already has full-time responsibilities and (2) the problem of financing rising costs of operation. It was decided to survey physicians and parents who had utilized the telephone information service concerning the value of the center to the medical profession and community. Also, findings were compared with those of a similar study[2] done in an area medically and geographically distinct from Omaha.

EVALUATION BY PHYSICIANS

A questionnaire was sent in November 1964 to the 527 members of the Omaha-Douglas County Medical Society requesting their opinion of the services rendered and their suggestions for improvement and financing. Of these questionnaires, 216 or 41% were returned. Since the physician's signature was not requested in order to allow him to express free criticism of the center, the distribution of respondents and nonrespondents could not be determined. The assumption was made that the respondents had more experience with or interest in the center than the nonrespondents. Among the respondents, approximately two-thirds had utilized the poison center at some time (Table 1). It is of interest that 143 of the responding physicians reported utilization of the center. The total number of Omaha physicians listed as general practitioners or pediatricians, the 2 groups most likely to use the center, is 131—suggesting wide acquaintance with the center by the medical profession.

Primary value. Physicians were asked what they considered the principal value of the center. As noted in Table 2, about two-thirds felt that information for physicians was primary, with half agreeing that information for parents was the secondary purpose of the service.

Delay in reaching the center. Because the residents taking the calls have numerous duties and are not at one fixed telephone, there was much concern that the delay in responding to telephone inquiries might be considerable. However, only 8.2% of the physicians who had utilized the center reported a significant delay (Table 3).

Satisfaction with services. The physicians were then given a choice of 3 paired descriptions concerning their opinion of how their inquiry had been handled: prompt vs. fumbled with sources; concise vs. too much discussion; correct vs. doubtfully correct. Any reply with 1 negative response was classified as unsatisfactory. Of the physicians who had called the center, 88.5% found the service satisfactory (Table 4). Comparison of responses with those given by Boston physicians showed little regional difference.

Some physicians reported very good service in which the resident had gone to considerable effort to obtain the answer. At the other extreme, the most distressing report was that in a sub-

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CAROL R. ANGLE *is assistant professor, pediatrics, University of Nebraska and Creighton University, Omaha, and* MATILDA S. MCINTIRE *is assistant professor, pediatrics and assistant research professor, neurology and psychiatry, University of Nebraska, Omaha.*

TABLE 1

PHYSICIAN UTILIZATION OF NEBRASKA CENTER

Utilization	*Physicians*	
Yes, called once in past year	27.6% (59)	
Called more than once	21.9% (45)	
Called previously, but not this year	18.7% (41)	
Have utilized at some time (total)		67.6% (143)
Never have utilized		32.4% (73)
Total		100 % (216)

TABLE 2

PHYSICIANS' OPINION OF PRIMARY VALUE OF CENTER

Primary value	*Physicians (216)*
Information for physicians	67.2%
Information for parents	7.3%
Increase in public awareness	6.9%
Publicity, resident training, and other	0.9%
No opinion	17.7%

TABLE 3

DELAY IN OBTAINING INFORMATION

	Physicians (143)	*Parents (77)*
No delay	91.4%	92.2%
Delay	8.2%	7.7%

TABLE 4

SATISFACTION WITH SERVICE

	Physicians		*Parents*	
	Omaha (143)	*Boston (446)*	*Omaha (77)*	*Boston (559)*
Satisfied	87.9%	81.3%	94.8%	90.9%
Dissatisfied	11.3%	1.7%	3.8%	2.9%
No answer	1.4%	17.0%	1.4%	6.2%

sequently fatal case of accidental poisoning due to gun bluing, a medical student had taken the call, was unable to find the information, and no further effort was made to obtain information.

Suggestions for improvement. Of the 143 physicians who had used the service, 52 had definite opinions on areas of improvement: 80% of these suggestions centered around improved personnel and telephone service; 13.4% concerned need for improved files and resource material; 7% concerned need for physician education. Since the time of this questionnaire, definite steps have been taken to follow these suggestions. The file space has been quadrupled. Secretarial time has been increased. Speakers have been offered to medical and lay groups, and other efforts in postgraduate education have been made.

Financing. Physicians were also presented with the problem that the operating budget of the center was about $6,000 per year (direct cost only) of which two-thirds was met by the hospital and the remainder by the Maternal and Child Health Services of the State of Nebraska. Most physicians, when asked if they had any suggestions for financing, felt that patient fees or donations (31.5%) or community donations (33.3%) were indicated. Grants were suggested by 22.8%, and city, county, or state appropriation of tax money by 12.2%. Several suggested combined sponsorship by organizations such as the area hospital council, medical society, and health department—a valuable suggestion for communities contemplating a poison control center.

EVALUATION BY PARENTS

In order to evaluate the telephone service given to the general public, 122 questionnaires were sent in November 1964 to parents who had called the center between Sept. 1, 1963 and Aug. 30, 1964, and for whom there was complete and legible information concerning the child, toxic substance, family residence, and telephone number. For a comparable one-year period, January through December 1964, 3.028 calls had actually been placed to the center through the hospital switchboard and 204 were reported to the National Clearinghouse. Of the 122 questionnaires, there were 77 replies. The distribution of age (96% ages 1 to 3 years), and sex (58% boys) was very similar for the 77 respondents and the total telephone reports for the calendar year 1964.[1] Analysis of the substances ingested (Figure) shows a slightly higher incidence of innocuous and miscellaneous substances suggesting less guilt than pride in making an unusual inquiry.

Source of information about the center. Previous articles had appeared in the Omaha newspapers and there had been considerable television and radio publicity about the Center. It was,

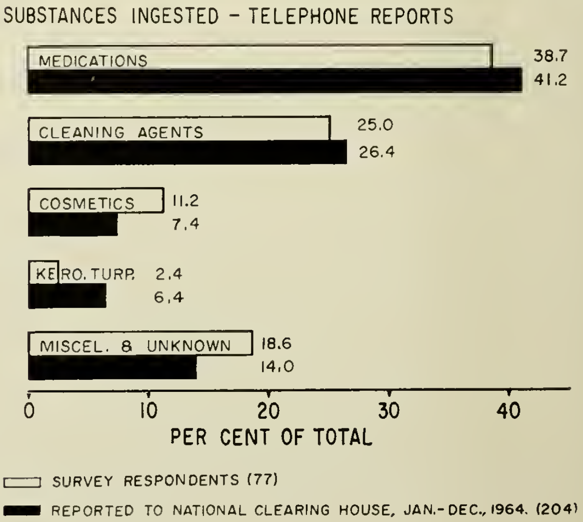

TABLE 5

SUGGESTIONS FOR FINANCING

Suggestions	*Physicians (58)*
Patient fee or donations	31.5%
Community services and donations	33.3%
Grants—industrial, drug, or U.S.P.H.S.	22.8%
Taxation—city, county, or state appropriation	12.2%

TABLE 6

PARENTS' SOURCE OF INFORMATION CONCERNING CENTER

	Boston	*Omaha*	*No.*
Physician	29.1%	29.1%	32
Friends	20.2%	23.6%	26
Newspaper	12.3%	15.4%	17
Telephone book	6.2%	9.1%	10
Radio, television	2.8%	11.8%	13
Other	21.4%	10.9%	12
No answer	7.9%	0	0
	99.8%	99.9%	110*

*33 gave more than 1 source

TABLE 7

PARENTS' CALLS TO PHYSICIANS AS WELL AS TO CENTER

	Yes	*No*	*No answer*
Called M.D. first	36.3%	58.4%	5.3%
Called M.D. later	15.5%	80.5%	4 %
Called M.D. on advice of center	9 %		

therefore, of interest to find that in Omaha, as in Boston, 29.1% of the parents reported the physician as their source of information. A striking consistency in the various other sources of information is also reported for the 2 cities (Table 6). In Omaha, the "other sources" were almost entirely paramedical: mother's clubs, clinics, nurses, and the like. Surprisingly, despite extensive use of mass media to publicize the center, 63.6% reported that they had heard of it by word-of-mouth. Concerning delay in getting information and satisfaction with service, responses from physicians and parents (Tables 3 and 4) were comparable to the Boston study except for higher percentage of respondents in our survey.

Primary calls. One of the major problems in the operation of a poison information center, as in the operation of a hospital emergency room, is that patients utilize these facilities directly without consultation with their family physician. The stated policy of the center has been to ask the parents if they have already called their physician. If not, they are instructed to call their physician but first aid advice is given where it seems indicated or if the physician is not available. In the questionnaire, the parents were asked if they had tried to call their physician before calling the center and also whether they had called their physician after receiving their initial information from the center. The majority (Table 7) relied on the center's information. Of those who later called their physician, over half did so on the center's recommendation.

Impact of safety consciousness. The parents were asked whether the occurrence of the accidental poisoning had made them more careful about possible poisonings. Although only 5 of the 77 families admitted not being more careful, 6 reported subsequent accidental poisonings. One family reported 2 more poisonings involving a 2½-year-old boy who would be an obvious subject for a study of a poison "repeater."[3]

In response to a question concerning accidents of any kind severe enough to require a physician's attention in the interim of 1 to 13 months since the poisoning incident, 19 (25%) of the families reported 1 or more accidents. The fact that all 5 families admitting no increase in safety consciousness following the accidental poisoning were in this group of 19 families suggests the potential use of accidental poisoning in a child as an index case for the accident-prone family.

SUMMARY AND CONCLUSIONS

A reasonably high level of satisfaction with services of a poison information center was shown in questionnaire returns by physicians and parents.

The majority of suggestions called for improved personnel and resource material: periodic evaluations and quality control seem imperative to justify the high operational costs.

Need for continuing education in toxicology was expressed by responding physicians.

The occurrence of other accidents in families after accidental poisoning suggests these children as index cases of accident-prone families.

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Congenital Cardiac Defects, a Genetic Viewpoint

PAUL K. MOORING, M.D., F.A.A.P.
Omaha

Over 1,000 different congenital defects can be found in human beings. One of 16 newborn infants has some type of congenital defect—be it structural, cellular, or metabolic.

Defects involving the heart, of course, represent only a small fraction of this impressive number of conditions. Yet, the heart occupies a unique position in life. Therefore, a discussion of congenital heart defects and their relationship to chromosomal and genetic abnormalities is appropriate.

Rather than discuss the nature of the most common cardiac defects, the following is a discussion of some of the genetics of the garden variety of cardiac defects. Also included are the cardiac manifestations of some less common congenital syndromes, more of which are being recognized every day.

INCIDENCE

The true incidence of congenital cardiac defects is not known in spite of several studies. Most estimates are probably low, considering that some defects, such as mild aortic stenosis and atrial septal defect, may not manifest themselves for many years.

Richards and her associates[1] in New York reported an incidence of 0.83% (8 out of 1,000) congenital cardiac defects in 6,000 infants, including stillbirths. MacMahon and co-workers[2] and Pleydell,[3] both in England, reported an incidence of 0.3% (3 out of 1,000). Of interest also in MacMahon's report, which was written in 1953 before open-heart surgery, was an incidence of congenital heart disease at 10 years of age of only 1 in 1,000. Thus, two-thirds had died in the first 10 years of life. In general, cardiovascular anomalies account for about half of the deaths in the first year due to congenital defects.[4]

Of the approximately 4 million babies born in the United States each year, somewhere between 12,000 and 32,000 will have congenital cardiac defects. Probably half of these will not survive, although many could be saved by prompt recognition and treatment.

EMBRYOLOGY

At three weeks' gestational age, the embryo is some 2 to 3 mm. or 1/10 in. long. The heart, just beginning to beat, consists of a straight tube which can be separated into 4 chambers: sinus venosus, atrial canal, ventricular canal, and bulbus cordis. Between now and the eighth gestational week, while the embryo grows to 28 to 30 mm. or slightly over 1 in., this straight tube will undergo elaborate turning and kinking, growing the atrial and ventricular septums, and will develop a separate pulmonary artery and aorta as well as 4 sets of delicate valves—and all the time this heart is effectively beating!

Certainly, this is a fabulous accomplishment. It is hardly any wonder that, for one reason or another, all of this does not come off on schedule and somewhat less than 1 out of 100 have defects. The great wonder is that over 99% develop correctly!

Significant in this development is that, if defects of the heart are going to occur due to chemicals, radiation, virus infections, or other unknown factors, they will have to have their deleterious effect before the second gestational month is over.[5] By the third month, the heart has pretty well completed its differentiation. From then on, it merely gets larger until the major circulatory changes during the early hours and days after delivery.

GARDEN VARIETY DEFECTS

Etiology. The majority of congenital cardiac defects—probably at least 9 out of 10—are unassociated with any recognizable syndrome or genetic anomaly. The major cardiac defects do not tend

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PAUL K. MOORING *is associate professor of pediatrics, and director of pediatric cardiology, University of Nebraska College of Medicine, Omaha.*

to be either familial or part of complex syndromes.

Associated defects, which are not part of recognized syndromes, occur commonly with congenital heart defects. Boesen and associates[6] found an incidence of 11% associated defects in a series of 615 children seen with heart defects and an incidence of 13.5% in 1,145 autopsied children with heart defects. Not included as an associated defect was mongolism, which was found in 4.7% of the clinical series and 11.8% of the autopsied series. Several other findings also were interesting. They noted that associated noncardiac defects rarely occurred with transposition of the great vessels, tricuspid atresia, or single ventricle. Tetralogy of Fallot defects usually were associated with gastrointestinal malformations (7%), ventricular septal defects with bone and joint malformations (5%), and atrial septal defects with cleft lip and palates (10%). Overall, the most frequent associated defects were gastrointestinal, followed by urogenital and bone or joint.

Such association of multiple organ malformation does not, as yet, help in elucidating the etiology of congenital heart defects other than to indicate that these organ systems are all being formed and, therefore, are most susceptible to various harmful agents or environmental conditions at about the same gestational age.

What do we know of the etiology of congenital cardiac defects? Unfortunately, very little as yet. The importance of maternal infection, of course, has been well demonstrated by the frequent findings of cardiac defects following maternal rubella during the first trimester, and especially the first two months of pregnancy.[7] Commonly, children born after such infections will have congenital heart defects in addition to deafness, mental retardation, or eye defects. The most common cardiac defect after maternal rubella is patent ductus arteriosus, but atrial septal defects, ventricular septal defects, pulmonary stenosis, and tetralogy of Fallot also occur. Mumps in utero has now been implicated as a possible cause of endocardial fibroelastosis since most infants with this condition have positive skin tests to mumps antigen. This, however, may be related to something other than mumps, because most infants do not have detectable serum antibodies to mumps virus.[8]

Drugs. What effects do drugs taken during pregnancy have on the development of congenital heart defects? Well known are the teratogenetic effects of thalidomide. Although cardiac malformations were not the chief malformations found after maternal use of this drug, many infants did have defective hearts. Most common have been ventricular septal defects, but tetralogy of Fallot, atrial septal defect, truncus arteriosus, and patent ductus arteriosus also have been reported. Most of these cardiac deformities were produced with thalidomide intake between the fortieth and forty-fifth days of pregnancy. Animal experiments[9,10] have shown that such noxious stimuli as maternal anoxia or vitamin deficiencies (especially vitamin A) often lead to cardiac defects in the offspring. Of interest is the drug, trypan blue, which, when given during pregnancies, tends to cause offspring with tetralogy of Fallot. These drug effects would be compatible with one theory of the cause of congenital cardiac defects, that is, malfunctioning of a vital but temporary enzyme system needed during organogenesis.[11]

Genetics. What is known of a genetic etiology for these common garden variety congenital cardiac defects? Again, not a great deal.

The increased incidence of associated defects with congenital heart defects, previously mentioned, could be due to either genetic anomalies or other prenatal disturbances. Studies of monozygotic twins show that the concordance rate for congenital cardiac defects is very low.[12]

There is, however, a small but distinct increase of heart defects in siblings, and probably in parents, of children with congenital heart defects when compared with the normal population. While the incidence in the general population is from 0.4 to 0.8%, for these close relatives the frequency is from 2 to 3%.[13,14] Frequently, these cardiac defects in relatives will be the same.[5] There now are many pedigrees of families with a high frequency of patent ductus arteriosus and atrial septal defects. We have followed one family with patent ductus arteriosus through 3 generations, and we noted 2 families with 2 children having tetralogy of Fallot or atrial septal defects. Lynch and associates[15] recently reported an instance of transposition of the great vessels occurring in siblings.

An interesting facet of the genetic factors involved in congenital heart disease is the findings in various lower animal species—especially the results of some breeding experiments.

As summarized recently by Detweiler,[16] congenital heart disease is far from uncommon in certain species, and particularly in dogs. Of 5,000 dogs screened for heart disease, 1% were found to have such defects. The frequency in purebred dogs was twice that of mixed breeds. Subaortic stenosis was common and almost always occurred in either boxers or German shepherds. Of great interest are highly inbred strains of brown leghorn chickens, over three-fourths of which have ventricular septal defects. By crossbreeding some low-incidence strains to these high-incidence strains, a drop in frequency was observed. These results are compatible with a genetic etiology.

Certainly, in some instances at least, genetic mechanisms are important in determining congenital heart disease. Perhaps, as McKusick has stated,[12] it is polygenetic and multifactoral, that is, involving several genes but modified by the prenatal environment.

On the basis of the information available, however, we usually feel confident in telling parents of children with congenital heart disease that there is little likelihood that subsequent children will be afflicted. The chance is about 1 in 50. If 2 children have already been affected, the chance of subsequent children having a defective heart is estimated to be 1 in 20.[17]

SINGLE GENE MUTANTS WITH CARDIAC DEFECTS

A large number of single gene disturbances have now been identified, and many have associated congenital cardiovascular defects as an integral part of the syndrome. All different modes of inheritance have been implicated.

In the group of connective tissue genetic disorders, one of the best known although least understood is the Marfan syndrome.[18] This well-known syndrome of excessive height and long spider-like extremities, with skeletal and eye defects (especially subluxated lens), is considered a mesodermal dystrophy. Due to stretching of the aortic valve ring, aortic insufficiency develops not uncommonly—sometimes as early as 5 years of age. Dissecting aortic aneurysms are also common. Pulmonary and, rarely, mitral insufficiencies also have been noted. This disorder is usually transmitted as an autosomal dominant but sporadic cases also occur.

Five genetic disturbances of mucopolysaccharides have now been described.[19] Three of these are associated with cardiac disturbances: the well-known Hurler's syndrome and the lesser known Morquio-Ullrich and Scheie's syndromes.

Hurler's syndrome, or gargoylism, is a mucopolysaccharidosis in which excessive amounts of mucopolysaccharides (chondroitin sulfate B and heparitin sulfate) are both excreted in the urine and deposited in various tissues. Characteristically, these patients are mentally retarded and dwarfed, with deformed bones, kyphosis, and cloudy corneas. Cardiac lesions are due to the excessive mucopolysaccharide deposits in coronary arteries and heart valves. Various murmurs and symptoms occur. Heart failure and cardiac deaths are common. Transmission has been established both as an autosomal recessive and sex-linked recessive.

Less common is the Morquio-Ullrich syndrome, now identified as mucopolysaccharidosis IV. The mucopolysaccharide excreted in this disorder is keratosulfate. The disease is inherited as an autosomal recessive. The clinical picture of this syndrome, which somewhat resembles severe rickets, is striking. Dwarfism is evident, as are a normal-sized but rigid head and trunk, kyphotic chest, and cloudy corneas. Intelligence usually is not impaired. By the teen years, almost all these children have aortic insufficiency, the cause of which is not clear.

Mucopolysaccharidosis V was just described in 1962 by Scheie and colleagues. This new syndrome, the Scheie syndrome, is transmitted as an autosomal recessive and also involves an excessive excretion of chondroitin sulfate B. Typically, these patients have stiffened joints, broad-mouth facies, excessive body hair, cloudy corneas, and normal intelligence. They, like those with the Morquio-Ullrich syndrome, also develop aortic insufficiency, frequently in childhood. The reason for this is not clear.

NEUROLOGICAL AND MUSCULAR DISORDERS

Several single-gene mutants involving primarily the neurological and muscular systems also frequently involve the cardiovascular system.

Friedreich's ataxia, a familial disease involving both the central nervous system and skeleton, also usually involves the heart. The electrocardiogram typically shows severe T-wave changes throughout the electrocardiogram, but particularly over the left ventricle. Arrhythmias also occur. Postmortem examinations show rather diffuse myocardial fibrosis.

Progressive muscular dystrophy—another familial disease—is transmitted as a sex-linked or single recessive gene disturbance. The heart is involved with the same degenerative process as the skeletal muscles, although frequently to a lesser extent. Various reports indicate one-half to three-fourths of these children have myocardial involvement. Clinically, cardiac involvement is manifested by cardiac enlargement, arrhythmias, abnormal T and Q waves, and heart failure. The heart failure in this instance usually will respond, for a while at least, to digitalis.

Interesting is another single-gene, primarily neurological disturbance—the Riley-Day syndrome or familial dysautonomia.[20] Inherited as an autosomal recessive gene and usually only in those of Jewish extraction, this syndrome is characterized by many autonomic disturbances. They include lack of tears, vomiting episodes, blotchy skin, and emotional and temperature lability, to name a few. The cardiovascular problems are related to deficient autonomic control of blood pressure with orthostatic hypotension and, less commonly, episodic hypertension.

PHAKOMATOSES

Three of the congenital neuroectodermoses have cardiovascular manifestations of importance. They are characterized by a tendency to run in families, apparently due to inheritance of an autosomal dominant.

Tuberous sclerosis,[21] although rare, is always remembered because of its association with a relatively rare cardiac malformation. This disease, characterized by its typical pink-brown papules in a butterfly distribution on the face (adenoma sabaceum) plus severe mental retardation and seizures frequently also has intramural cardiac tumors. These rhabdomyomas tend to cause cardiac enlargement, arrhythmias, and severe conduction disturbances. Since they are multiple and intramural, they are inoperable.

Von Recklinghausen's disease[21] (neurofibromatosis) and von Hippel-Lindau's syndrome[12] (angiomatosis) have been found to be associated with pheochromocytomas. Pheochromocytomas also may occur as isolated familial defects.

INBORN ERRORS OF METABOLISM

Another inborn error of metabolism with cardiac manifestation occurring as a familial, and sometimes sex-linked, disease is glycogen storage disease.[5,22] Of the four types now known, only type II (Pompe's disease) characteristically involves the heart to a severe degree. Type III occasionally involves the heart.

Contrasted with children who have type I, or von Gierke's disease, and who may have a huge liver and an almost normal-sized heart, in type II, or cardiac glycogen storage disease, there is a huge heart and little liver enlargement. Usually no murmurs are present, and severe left ventricular hypertrophy, with ST-T wave changes, is noted in the electrocardiogram. Most infants die before 8 months of age.

SYNDROMES WITH CARDIAC MALFORMATIONS

There are several rather complex syndromes which are apparently determined by single gene disturbances and which usually have cardiac defects.

Kartagener's syndrome,[23] often familial, consists of the triad of chronic sinusitis, bronchietasis, and dextrocardia with situs inversus.

The recently reported Holt-Oram or atriodigital syndrome[24] also belongs in this group. This condition, which has been traced through 4 generations, consists of abnormal thumbs, in which the thumb lies in same plane as the fingers, with a rudimental middle phalanx of thumb. Terminal phalanges curve inward, and scaphoid deformities and high arched palates also occur. Atrial arrhythmias have been conspicuous. The cardiac defect is a secundum atrial septal defect.

The most complex of this group is the Ellis-van Creveld syndrome,[12,25] a disease transmitted as an autosomal recessive. Many pedigrees are available for this condition, particularly a large number in the isolated Amish communities of Pennsylvania. Sometimes classified a chondroectodermal dysplasia, this syndrome consists of chondrodystrophic dwarfism; polydactyly; deformities of fingernails, toenails, and teeth; and a peculiar "partial harelip." Somewhere from 50 to 60% have congenital cardiac defects. Most frequently, this is the rather unusual defect of a single atrium.

There are a number of other cardiac defects which are sometimes familial and presumably the results of single gene mutants. Four of these are not uncommon. These are endocardial fibroelastosis, idiopathic familial myocardiopathy, muscular subaortic stenosis, and supravalvular aortic stenosis.[12] These defects are usually not associated with other organ malformations.

Supravalvular aortic stenosis is particularly interesting, in that two genetic forms are recognized. In one group, this defect tends to occur as an isolated defect but has a familial tendency. The other group, in which the identical heart defects occurs in a sporadic form, is associated with a typical facial appearance, small head, and moderate mental retardation. These children, who do not look like their siblings but resemble each other closely, have full faces, broad foreheads with hypertelorism, heavy cheeks, wide mouths with full lips, and pointed chins.

CHROMOSOMAL ABNORMALITIES

No chromosomal abnormality has been detected for any of the conditions already mentioned except one instance of a mosaic trisomy 19 for supravalvular aortic stenosis.[26] Single gene disturbances, of course, would not be expected to be detected with the present state of the art of cytogenetics.

Four of the recognized chromosomal anomalies have heart defects as a characteristic aspect of their clinical picture. The best known, of course, is mongolism or, preferably, Down's syndrome (trisomy 21).[27] As is so well known, congenital heart disease is extremely common in this autosomal trisomy. Approximately one-third are found to have defective hearts. Typically, this defect is one involving the endocardial cushion, that is, septum primum defect or atrioventricular canal. This cardiac defect has the unusual and characteristic electrocardiogram which shows a left axis in the standard leads but right ventricular hypertrophy in the precordial leads. Various surveys have shown that, of the children with Down's syndrome and defective hearts, about one-third will have endocardial cushion defects, one-third will have ventricular septal defects, and the remaining third, secundum atrial septal defects and miscellaneous defects. Of interest is the great rarity in Down's syndrome of two rather common defects—transposition of the great vessels and coarctation of the aorta.

The autosomal trisomy of chromosome 13-15 (trisomy D_1),[28] first recognized in 1960, occurs about once in every 2,000 births. This condition is characterized by low birth weight, with severe deformities of eyes, ears, brain, and hands. Typically, these infants also have cardiac defects —usually ventricular septal defects—frequently with dextrocardia.

Trisomy E, an extra autosome of the 17-18 group,[29] usually produces a picture somewhat less conspicuous than the other trisomies mentioned. With a frequency of 1 in 1,000, this condition is also characterized by low birth weight with mental and physical retardation. Flexion deformities of the fingers and rocker-bottom feet usually are present. The cardiac defect associated with this trisomy condition is usually a ventricular septal defect with or without patent ductus arteriosus. Of interest is a group of 3 patients reported in 1963 by Townes and associates[30] in which all 3 infants with trisomy E had strikingly similar cardiac defects—a large posteriorly situated membranous ventricular septal defect and moderate valvular pulmonary stenosis with redundant bicuspid values.

Last among the common chromosomal anomalies characteristically affecting the heart is Turner's syndrome[31] or XO (sometimes called Bonnevie-Ullrich syndrome). This defect, occurring once in 3,000 births, classically is associated with coarctation of the aorta. A few have pulmonary stenosis and some have had hypertension without demonstrable coarctations. Perplexing is the severe edema of the hands and feet noted at birth in some infants with Turner's syndrome.

For reasons that are not clear, two of the chromosomal aberrations—Klinefelter (XXY) and the triple X (or super female) syndromes—have not been associated with an increased incidence of congenital cardiovascular defects.[12] This raises interesting questions as to why the absence of an X or Y chromosome in Turner's syndrome would have such deleterious cardiovascular effects, but the presence of an extra X chromosome apparently has no such effects.

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Radiation Factors in Congenital Malformations

RICHARD E. OGBORN, M.D., and MERTON A. QUAIFE, M.D.
Omaha

LAYMEN AND SCIENTISTS are disturbed by the widespread dissemination of half-truths concerning the effects of radiation on biological systems.

To disseminate knowledge requires acquisition, study, interpretation, and publishing of facts. Therefore, effort should be made to dissuade irresponsible professional and lay people from reporting half-truths and emotional statements about radiation.

To restrict the scope of this paper to a more responsible level, the discussion will be limited to the effect of ionizing radiation upon the stages of embryonic development as opposed to the effect on germ cells or their primordia.

To undertake such an investigation of the effect on the embryo, one may follow a general outline, such as:

1] Sources of radiation
2] Probabilities of interaction of radiation and the embryo
3] Reaction itself
4] Resultant effects
5] Preventive measures to reduce harmful effects.

SOURCES

Sources may be divided into natural or unavoidable (Table 1), medical, industrial, military, and miscellaneous.

Increased diagnostic utilization of radiation (Table 2) challenges the physician to be cognizant of the potential hazard and to employ only those methods which will divulge the greatest information with the least exposure.

TABLE 1
SOURCES OF UNAVOIDABLE RADIATION

Source	*Yearly exposure**
Radiocarbon in body	1.5 mr.
Radiopotassium in body	20.0 mr.
Cosmic rays at sea level	35.0 mr.
at 5,000 feet	50.0 mr.
Earth background	100.0 mr.

*Approximate averages from various sources

TABLE 2
MEDICAL SOURCES OF RADIATION

Source	*Exposure*
Chest X-ray	50 mr.
Chest photofluorograph	1,000 mr.
Lumbar spine (anteroposterior)	1,500 mr.
Lumbar spine (lateral)	5,700 mr.
Fluoroscopy recommended	1,000 mr. per minute

Industrial sources, including accelerators, power reactors, and radioactive isotopes, are increasing daily. The Third International Conference on Peaceful Uses of Atomic Energy held in Geneva, Switzerland, in September 1964 focused attention upon the rapid world-wide increase in the use of atomic energy. Desalination of sea or brackish water by flash boiling in nuclear reactors is being used. The economic production of pure water and electricity by this method prophesies world-wide use within ten to fifteen years. The destruction of insects harmful to domestic animals and crops by radiation has been successfully achieved in Florida and Greece.[1] Naval ships of various types are now powered with nuclear reactors, and many countries have designs for such ships in their future merchant marine fleets.[2] The metal and oil industries commonly use radioactive materials for production control today.

In delivering the summary address to the Atoms for Peace Conference in 1964, Dr. Glenn T. Seaborg stated: "By the turn of the century,

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RICHARD E. OGBORN *is associate professor of nuclear medicine, Department of Radiology, University of Nebraska College of Medicine, and chief of staff, Veterans Administration Hospital, Omaha.* MERTON A. QUAIFE *is instructor in internal medicine, University of Nebraska College of Medicine, and chief, Special Laboratory for Nuclear Medicine, Veterans Administration Hospital, Omaha.*

our Conference suggests more than half of the world's electricity will be generated by nuclear energy."[3] Added to this method of producing electricity, such techniques as nuclear thermoelectric and thermoionic conversion open new avenues for power generation. All these industrial usages open possibilities of radiation exposure to the embryo. At present, only a small proportion of the world population is exposed and, in general, the precautions taken in the industrial field represent the greatest achievement in industrial safety to date.

In the future, as greater opportunity for exposure exists, physicians will have a more critical need to know of the science of radiobiology. A large segment of the population in the reproductive age range will be involved in this expansion of the use of atomic energy in industry.

Military utilization of atomic energy, with the resultant possibility of exposure to radiation, is assuming greater importance. In spite of the fact that weapons testing and use have been curtailed at present, the increase in atomic-powered ships and submarines, the development of nuclear spaceship propulsion, and the development of electrical power systems for remotely based troops are continuing. In the research, development, manufacture, and usage of these items, more people will be exposed to radiation. The exposure will include those people in the reproductive age range, which is similar to the industrial and military ranges.

A fifth source of radiation may be called miscellaneous, useful, and nonuseful. Research utilization and shoe-fitting flouroscopic instruments serve as examples.

INTERACTION

The sources of radiation are numerous. The possibilities of interaction with pregnant women, however, can be rigidly controlled in 4 of the 5 categories, namely, industrial, medical, military, and miscellaneous. To have rigid control, however, means the assumption of greater responsibility of industrial, military, and civilian physicians. Through legislation and conscience, the elimination or reduction of exposure of women in the child-bearing age to these sources may be accomplished.

The next step in acquiring whole truth is to look at the interaction of radiation with biological matter. In the last two decades, there has not been a paucity of literature available. On the contrary, so much refuse has been accumulated that it is discouraging to attempt collection, triage, and integration of the facts presented.

Roberts Rugh has presented a summary of known facts concerning the interaction of radiation and embryos.[4] This summary followed an exhaustive search of the literature as well as personal research. The whole is masterfully integrated and presents our current knowledge in this area.

A curtailed summary of this work reveals that the damaging effects of radiation are noted primarily on the nucleus and chromosomes. The fertilized cell is more sensitive than either gamete. The embryo is most radiosensitive in an early embryonic stage of development. Certain anomalies can be produced only during embryonic and fetal life. There is no evidence which supports recovery of embryonic cells from the effects of irradiation. The differentiating cell is the most radiosensitive, and yet differentiation of cell or organ may occur before there is histologic evidence of its appearance. Damage to cells by radiation will result in deficiencies of the embryo. Primitive cells may be directed within limits of the ability of the organism to compensate for these deficiencies, but the irradiated embryo will develop inadequately. Similar anomalies may be produced in any vertebrate embryo by ionizing radiation. Death of the embryo is achieved by the effects of radiation on vital organ systems. Diagnostic exposures may cause severe deficiencies in certain early stages of the central nervous system. Other factors may cause congenital malformations, yet irradiation, because of its unique character, should be avoided. All physicians are strongly advised to read and reread Rugh's classical review of interaction of radiation and the embryo.

EFFECTS

To further acquire knowledge, it is necessary to review the effects of radiation on the embryo. Death with resorption characterizes one end of a spectrum of radiation insult to the embryo. Marked effects have included such results as anencephaly, cerebral atrophy, mongolism, mental retardation, and cerebral palsy. Almost the complete spectrum of eye abnormalities, from anophthalmia to partial albinism, has been observed. Skeletal deformities include odontogenesis imperfecta, abnormal limbs and feet, congenital dislocation of hips, vaulted cranium, and universal reduction of the skeleton as a whole. Other systems are equally affected, with, for example, absence of kidney, degenerate gonads, congenital heart disease, and pituitary irregularities. Irradiation of the embryo may produce deficiencies within any system, varying from complete disorganization to minimal unrecognizable defects. The most sensitive period is during differentiation of the cells or the organs of that system. Rugh[5] summarizes the critical time periods relative to incidence of pre- and neonatal death and abnormal individuals in mice. He then extrapolates this data to man, including the data regarding congenital malformations due to irradiation of human beings. His data and extrapolations support others in revealing the exquisite radiosensitivity of the embryo.

The true facts known today regarding the sources, interaction, and effects of irradiation on the embryo are sufficient to allow the responsible physician to utilize this knowledge in the prevention of many congenital malformations by eliminating or drastically reducing exposure of the woman of childbearing age to radiation. One extra aspirin or one extra photon is negligence. One aspirin or one X-ray film not obtained when necessary is negligence. Unnecessary exposure of these females to industrial, military, or miscellaneous irradiation can and will increase the probabilities of congenitally malformed infants.

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Central Language Disorders as Seen in a Mental Retardation Evaluation Clinic

MATILDA McINTIRE, M.D., JOHN WILEY, Ph.D.,
and WILLIAM WOLSKI, Ph.D.

Omaha

The incidence of communicative disorders in retarded children is high, as indicated in a number of studies.[1] As might be expected, speech and language development is delayed in the majority of these children. Irwin's studies[2,3] have indicated that speech sound development is related more closely to mental age than to chronological age. Other aspects of speech and language behavior in the retarded have been studied. Within a larger group of children referred to the Nebraska Psychiatric Institute for evaluation of their retardation, several subgroups have emerged on the basis of their presenting aberrant communicative behavior. One of these groups to become a focus of interest consists of children with an apparent central language disorder. Initially, central language disorder has been defined here as failure to develop expression and understanding of language symbols, but with essentially normal hearing sensitivity.

The relationship of speech and language disorders to neurological deficits has been an area of interest for many investigators in neurology, psychology, pediatrics, education, and other fields.[4–9] Much has been learned about the human brain from the study of aphasia. While the literature is extensive, relatively little has been devoted to the subject of congenital or developmental language disorders in children. Whether or not these disorders can be properly labeled as aphasia has been a subject of controversy. Since there is an area of disagreement, we have preferred to use the designation of central language disorders for the children described in this study.

Central language problems are among the more baffling of the communicative disorders. They have been defined further as a language disorder which cannot be accounted for by damage to or malfunction of the peripheral nervous system. It is the purpose of this paper to report on thirty-five of these children referred originally to the Mental Retardation Evaluation Clinic at the Nebraska Psychiatric Institute. These children were all referred because someone—family physician, school personnel, parents, and so on—thought that they might be mentally retarded. A total of 792 infants and children were seen from July 1958 to June 1964. Thirty-five of these were diagnosed as having as their major problem a central language disorder. Twenty-eight of these children who were seen before June 1963 were described in a paper presented in 1964.[10]

The multidiscipline method of evaluation was used throughout this project. Each child was evaluated by a team consisting of a pediatrician, neurologist, psychiatrist, psychologist, speech pathologist, audiologist, and social worker. Routine laboratory tests consisted of complete blood count; urinalysis, including test of phenylketonuria; X-rays of the skull, chest, pelvis, and wrist; and an electroencephalogram. Additional studies as indicated were obtained from the University of Nebraska Medical Center. Some children were seen for only one evaluation, while others were seen several times. The results reported in this paper are on the basis of the initial evaluation only. Concurrent with patient evaluations, staff conferences were held, and diagnoses and recommendations were made. These findings were relayed to the parents by means of interpretation interviews by staff members who had examined the child. Some families received psychiatric and other specialized services at the institute, while others were referred to outside agencies for treatment.

This clinic was concerned primarily with chil-

MATILDA MCINTIRE *is research assistant professor, Department of Neurology and Psychiatry,* JOHN WILEY *is associate professor of speech pathology, Department of Neurology and Psychiatry, and* WILLIAM WOLSKI *is instructor in speech and pathology, Department of Neurology and Psychiatry, University of Nebraska College of Medicine, Omaha.*

dren under the age of 6 years, and 627 or 79% of the 792 children evaluated were under 6 at the time of evaluation. Predominant presenting problems included unspecified slow development, speech problems, physical handicaps, convulsions, and behavior problems. Over two-thirds of the group had some motor dysfunction. The majority of the children exhibited some degree of mental retardation, although a few seemed to have above average ability.

As this project progressed, it was noted that some children seemed to have language abilities that were much inferior to their nonlanguage skills. Some seemed to hear but yet did not understand. Most seemed to be more responsive to visual stimuli than to auditory cues. Many did not talk. Separately, these children were identified by members of the communicative disorders team. As more of these children with specific language disabilities appeared, the authors began to look for a pattern of other characteristics, some of which are reported in this paper.

The group under discussion is predominantly male, with 27 males and 8 females. The median age at the time of evaluation was 5 years and 4 months, while the average when the parents first suspected the problem was between 2 and 3 years. The age at time of evaluation probably reflects the parents' concern about the child's poor speech when faced with impending school entrance.

The home environment of these children does not seem remarkable. Twenty-six were living with their own parents. Only five children were living in a one-parent family, and four children were living with stepparents. At the time of evaluation, the median age of the father was 33 years and the mother 29 years. Only eight of the fathers and seven of the mothers had not completed high school. Seven fathers and ten mothers had some college education.

The median income was approximately $5,000. The significance of this is difficult to ascertain as several factors may have influenced the applications for service in this program. Most programs at the Nebraska Psychiatric Institute are designed for families of limited income. Although no such income limitation existed for this program, applications may have been limited by the general policy of the Institute.

Table 1 describes the pregnancy, labor, and delivery characteristics of these children, together with their neonatal period, motor development, physical examination findings, and the results of the electroencephalograms.

In two-thirds of the cases, the pregnancy was normal. Pregnancy abnormalities included spotting, bleeding, hypertensive disorders, and two cases of German measles in the first trimester. There were no cases of blood incompatibilities. One case of hyperbilirubinemia was due to giant-cell hepatitis in a mother who had influenza during pregnancy. In the eleven abnormal pregnancies, only one of the children was normal on physical examination. Five of these children had an adjustment reaction.

In 85% of the cases, the labor was normal. The abnormalities consisted of the necessity to induce labor, prolonged labor, and one cesarean section.

Over three-fourths of the deliveries were normal. Abnormalities were primarily those of abnormal presentation or premature separation of the placenta. Data were not available in one case, since the child was adopted.

Slightly over half of these children had a normal neonatal period. Abnormalities included difficulties in breathing with cyanosis and difficulties in feeding. There was one case of neonatal meningitis and one of giant-cell hepatitis.

About half of the children had normal motor development. Delayed motor development was the primary abnormality. Differences between boys and girls were significant. While 18 of the 28 boys had normal motor development, only one of the seven girls had normal motor development. Physical examinations were normal in two-fifths of the cases. In the others, the abnormalities were primarily in the area of varying degrees of motor dysfunction and multiple congenital anomalies. Six of the eight girls had abnormal physical examinations. For this group, central language disorders in girls are accompanied by abnormal physical examinations and deviations in motor development.

Eighty-five percent of the children had normal electroencephalograms. Of the five with abnormal electroencephalograms, three showed abnormal focal spikes. In this group was the one child with a convulsive disorder. This child had had neonatal meningitis. All five abnormal electroencephalograms were found in the full-term boys. Although the majority of the girls had motor dysfunctions and abnormal physical examinations, all of them had normal electroencephalograms.

Table 2 summarizes the results of the psychological evaluations. Two-thirds of these children were not retarded on the nonverbal part of the psychological evaluation, while all were retarded with respect to verbal skills. Of the eleven who showed evidence of retardation in the nonverbal evaluation, eight had severe verbal disorders and three had moderate verbal disorders. In contrast, those who were not retarded in nonverbal abilities showed mild verbal disorders.

TABLE 1

PRENATAL, NATAL, AND POSTNATAL CHARACTERISTICS OF CENTRAL LANGUAGE DISORDER PATIENTS

	Males			*Females*			*Total group*		
	Full term	*Pre-matures*	*All males*	*Full term*	*Pre-matures*	*All females*	*Full term*	*Pre-matures*	*Group total*
Pregnancy									
Normal	17	2	19	4	1	5	21	3	24
Abnormal	6	2	8	1	2	3	7	4	11
Labor									
Normal	20	3	23	3	3	6	23	6	29
Abnormal	3	1	4	1*	0	1	4*	1	5*
Delivery									
Normal	20	2	22	2	2	4	22	4	26
Abnormal	3	2	5	2*	1	3	5	3	8*
Neonatal									
Normal	12	0	12	5	1	6	17	1	18
Abnormal	11	3*	14	0	2	2	11	5*	16*
Motor development									
Normal	17	1	18	1	0	1	18	0	18
Abnormal	6	4	10	4	3	7	10	7	17
Physical examination									
Normal	12	1	13	1	1	2	13	1	14
Abnormal	11	4	15	4	2	6	15	6	21
Electroencephalogram									
Normal	18	3*	21	5	3	8	23	6*	29*
Abnormal	5	0	5	0	0	0	5	0	5

*Incomplete data on one child

TABLE 2

PSYCHOLOGICAL TEST DATA, A COMPARISON OF VERBAL AND NONVERBAL SCORES

	Males			*Females*			*Total group*		
	Full term	*Pre-matures*	*Total males*	*Full term*	*Pre-matures*	*Total females*	*Full term*	*Pre-matures*	*Total group*
Verbal									
No mental retardation	0	0	0	0	0	0	0	0	0
Mild mental retardation	17	0	17	2	3	5	19	3	22
Moderate to severe	6	4	10	3	0	3	9	4	13
Indeterminate	0	0	0	0	0	0	0	0	0
Nonverbal									
No mental retardation	17	1	18	4	2	6	21	3	24
Mild mental retardation	6	3	9	0	0	0	6	3	9
Moderate to severe	0	0	0	1	0	1	1	0	1
Indeterminate	0	0	0	0	1	1	0	1	1

TABLE 3

HEARING DISORDERS IN CENTRAL LANGUAGE PROBLEMS

	Males			*Females*			*Total group*		
	Full term	*Pre-matures*	*Total males*	*Full term*	*Pre-matures*	*Total females*	*Full term*	*Pre-matures*	*Total group*
Hearing									
Adequate	18	2	20	4	1	5	22	3	25
Inadequate	2	1	3	1	1	2	3	2	5
Indeterminate	3	1	4	0	1	1	3	2	5

TABLE 4

SPEECH DISORDERS IN CENTRAL LANGUAGE PROBLEMS

	Males			*Females*			*Total group*		
	Full term	*Pre-matures*	*Total males*	*Full term*	*Pre-matures*	*Total females*	*Full term*	*Pre-matures*	*Total group*
Speech									
None	6	3	9	0	1	1	6	4	10
Inadequate	15	1	16	5	2	7	20	3	23
Acceptable	2	0	2	0	0	0	2	0	2

TABLE 5

PSYCHIATRIC DISORDERS IN CENTRAL LANGUAGE PROBLEMS

	Males			*Females*			*Total group*		
	Full term	*Pre-matures*	*Total males*	*Full term*	*Pre-matures*	*Total females*	*Full term*	*Pre-matures*	*Total group*
Psychiatric status									
Normal	16	4	20	3	2	5	19	6	25
Abnormal	7	0	7	2	1	3	9	1	10

Table 3 reports hearing testing results. There were twenty-five children with socially adequate hearing, five with definite hearing losses, and five who were indeterminate. Of the five children with definite hearing losses, one child was essentially normal on physical examination while the others showed definite abnormalities including von Recklinghausen's disease, multiple congenital malformations due to rubella in the first trimester, familial craniostenosis, and a birth weight of 2 lb. 14 oz. in one child. Thus, four of the five children with inadequate hearing showed low birth weight or marked physical abnormalities.

The data on speech and language evaluations are summarized in Table 4. Ten of the children had no speech. Nine of these were boys, and all but one showed evidence of motor dysfunction, birth injury, or major disease process.

Information presented in Table 5 indicates that over two-thirds of these children did not have psychiatric problems. All of the psychiatric disturbances were adjustment problems, except for one psychoneurosis. There were seven boys and three girls in this group. Clinically, many of the adjustment problems seemed related to the difficulties of confused and distraught parents in dealing with their bewildering offspring.

While there were complications during the prenatal, natal, and postnatal period in this group of thirty-five children, only two cases of rubella and no Rh blood incompatibilities were found. Goldstein, Landau, and Kleffner,[11,12] however, reported seven cases of rubella and four Rh incompatibilities in their population of 69 aphasic children.

Difficulties in labor occurred in less than one-sixth of the thirty-five children and difficulties in delivery in less than one-fourth of the group. More characteristic of this population were problems in neonatal development, motor dysfunction (usually mild), and abnormalities in the physical examination. Problems of motor function and physical integrity were characteristic of the girls but occurred in less than half of the boys. While less than 15% of the electroencephalograms in this group were abnormal, Goldstein, Landau, and Kleffner found 42% of the electroencephalograms abnormal in their sample of aphasic children. They concluded that their aphasic group was not uniform; one-half had moderately severe hearing losses and six had borderline mental retardation in repeated tests (p. 757). Our data also suggest that these children were not uniform, but for different reasons. In the Goldstein, Landau, and Kleffner study, children were referred for deafness and for language problems. Children in our group, however, were referred for evaluation of retardation. Common characteristics of the two groups include severe speech disorders, language deficiencies, essentially normal nonlanguage functioning, and a predominance of males. Further exploration is needed to answer important questions concerning etiology and other characteristics of these language-disorder children.

Two examples may serve to illustrate the complex nature of these problems. One male child, who was first examined at age three, was evaluated as a minimally diffusely brain-damaged child with a behavior reaction. In this case, the mother had rubella in the first trimester. There were two normal siblings, one older and one younger. The fourth pregnancy resulted in a miscarriage. This child was very difficult to test. He had no speech, very limited language, and a possible hearing loss. Previously, he had been considered deaf and autistic. Motor development was normal, but the child was below the third percentile in height and weight. Bone age was retarded. The electroencephalogram was normal. Following a brief period of treatment in the Children's Psychiatric Service, this child was referred for individual speech and language treatment. He was seen for six months, three times a week by the Communicative Disorders Section of the Nebraska Psychiatric Institute. During this period, his general behavior improved markedly, but communicative behavior changed little. A year and a half later, the child did not have any consistent communication with others, and he was placed in a children's unit in a psychiatric hospital. Although this child is able to do some nonlanguage tasks at normal levels, prognosis is poor.

Another child was seen at age four, following speech and language therapy. In this case, the speech pathologist referred the child for neurological evaluation. Electroencephalograms were abnormal. Psychological evaluation indicated better than average nonverbal skills, but with verbal skills at a 2-year level. He used gestures, pantomine, some words, and some jargon. His parents felt that he must have a hearing loss. First hearing tests were indeterminate, but later tests indicated socially adequate hearing. The child was placed in a kindergarten class where he made fair progress. The teacher talked to his parents several times about his hearing loss. A series of demonstrations convinced the parents that he could hear but could not understand what he heard. He was placed in a special program of language training at the Nebraska Psychiatric Institute during the summer, where he learned a number of language concepts. During the past year, he has attended first grade in a public school where his visual alertness, good social behavior, and nonlanguage skills have kept him going. His behavior has improved markedly since his parents have developed a better understanding of his problem.

SUMMARY

Thirty-five children are described with central language disorders (a failure to develop understanding or expression of language symbols with subsequent lack of normal speech with essentially normal hearing). There were 27 males and 8 females. Of this group, 20% or 4 boys and 3 girls had a birth weight below 2,500 gm. (5 lb. 8 oz.). Eighteen of the 28 boys had normal motor development, while only 1 of the 7 girls had normal motor development. Eighty-five percent of the children had normal electroencephalograms. Two-thirds of the children were not retarded on the nonverbal part of the psychological evaluation.

There is a small group of 5 children who had a hearing loss in addition to a central language disorder. Four of the five children showed physical abnormalities or a low birth weight.

As a group, these children with central language disorders exhibit specific disabilities in language and communicative skills. In many ways, they are not retarded. They may be regarded as such, however, or deaf or autistic, unless they are evaluated carefully. Additional papers are planned to discuss further evaluations and follow-up on this group of most interesting and often puzzling children.

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Familial Lymphoma

PERRY G. RIGBY, M.D., HARLAN L. PAPENFUSS, M.D.,
and HENRY M. LEMON, M.D.

Omaha

THE TITLE DENOTES a tragedy; this is a report of three out of five siblings who developed a lymphoproliferative malignancy during their childhood. This occurrence has challenged the total resources of family, physician, and medical community and has stimulated consideration of hereditary and environmental circumstances in this affected sibship. This may be considered a family "cluster" of the illness defined not only by time and geography but also by inheritance.

Recent investigations have highlighted the familial and cellular genetic patterns of hematologic malignancies.[1–8] The evidence concerning the role of infective microbiological agents—virus or pleuropneumonia-like organisms (PPLO)—in the etiology of these disorders mounts from the standpoints of epidemiology, immunology, human-animal transmission, and "virus-like" particle isolation.[9–17] The lumping together of leukemias and lymphomas and, in fact, lympho- and myeloproliferative disorders for purposes of etiologic consideration allows a broadly based view of the factors involved.[18–20] The interrelationships are many and are paralleled and expanded by animal malignancy virus models.[21,22] Many years of investigation of the leukoses of fowl and the various oncogenic viruses isolated from mice have shown that closely related viral strains may induce neoplastic alteration and proliferation of a wide variety of tissues.[22] These include fibroblasts, osteocytes, reticulum cells, lymphocytes, myelocytes, and plasma cells, with either local solid tumors or hematogenous invasion. Therefore, until more of the etiology of human leukemia and lymphoma is known, there is some reason for regarding many of the different clinical variants of disease expression as possibly affected by a common agent or group of agents derived from the environment.[23,24]

Much of this investigative effort has been applied to the leukemias for many reasons—availability, circumstance, interest, and so on. While the total number of lymphoma patients is comparable grossly to the leukemias in most areas, the occurrence of childhood lymphoma is considerably less common. The finding of a remarkably similar type in three children of one family is rare indeed. The Burkitt lymphoma which does occur in children, especially in certain areas of central Africa (though also well documented in the United States), has enhanced the interest in the epidemiologic and microbiologic investigation of these disorders.[25]

The following family represents one of the first and most striking aggregates of malignant lymphoid tumors in a kindred which we have thus far encountered while initiating a survey of hematologic malignancy in Nebraska.[26] The three familial lymphoma cases are presented below, and a discussion follows on the heredity and pathologic and epidemiologic features germane to this study.

CASE REPORTS

Case 1. R.W.S., a 3-year-old white male, was admitted to the Lincoln General Hospital (No. 60119) on April 7, 1947, with the complaint of a cough of one week's duration that was becoming progressively more severe. At the onset of the illness, vomiting and diarrhea were experienced, and there was a "slight" fever. During the two days before admission, he seemed to have difficulty in breathing at times, with respirations of a "grunting" character.

The patient had been delivered at this hospital at term on May 19, 1944, with birth weight of 8 lb. 9 oz. Delivery was uneventful, and postnatal development was normal. Because of frequent colds accompanied by cervical lymphadenopathy and nasal obstruction, tonsillectomy and adenoidectomy were performed on Feb. 14, 1947. No other history of ill health was obtained.

When examined at the time of admission, he appeared well developed and nourished but acutely ill. Although cyanosis was not detected, respiratory distress was evident with breathing of a "grunting" nature. No abnormalities of the ears, eyes, nose, or throat were detected. There was no cervical lymphadenopathy. The thorax was symmetrical but with a distinct lag on the left. Dullness on percussion, decreased breath sounds, and numerous

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PERRY G. RIGBY *is assistant professor of internal medicine,* HARLAN L. PAPENFUSS *is assistant professor of pathology, and* HENRY M. LEMON *is director, Eppley Institute for Research in Cancer and Allied Disease, University of Nebraska College of Medicine, Omaha.*

fine inspiratory rales were noted over the left lung. No abnormalities of the heart or abdomen were noted. The hemoglobin was 11.6 gm. per 100 ml. and the white cell count 11,750 per cubic millimeter with 57% segmented neutrophils, 3% neutrophils, 38% lymphocytes, and 2% monocytes. An X-ray film of the chest showed a massive left pleural effusion with displacement of the heart and mediastinal structures to the right. In lateral projection, the effusion seemed to be limited anteriorly.

On the third hospital day, 450 ml. of turbid straw-colored fluid was aspirated from the left pleural cavity. Despite penicillin and symptomatic and supportive therapy, repeated thoracenteses were necessary. Terminally, cyanosis and progressive edema of the face, neck, thorax, and upper extremities developed. He died May 5, 1947.

At autopsy, the body appeared to be that of a well-developed and nourished male. Size and weight were considered normal for the stated age. There was marked bilateral hydrothorax with the right pleural cavity containing an estimated 250 ml. of turbid fluid and the left, 400 ml. of a similar fluid. A large, firm, gray-white neoplasm occupied the entire anterior mediastinum. The tumor extended to surround the pericardial sac down to the diaphragmatic attachment. There was also extension upward to surround the arch of the aorta and the vessels at the base of the neck. The structures at the hilus of each lung were incorporated within the tumor mass, but there was no extension into the pulmonary parenchyma. Posterior mediastinal structures, including the trachea and esophagus, were displaced but not surrounded by the neoplasm. No recognizable thymic tissue was detected. On section, the tumor was composed of homogeneous, gray-white tissue. Both lungs were congested and contained areas of atelectasis and consolidation. The heart was normal in size and configuration. The spleen was enlarged to 55 gm. and congested with the follicular markings accentuated. There was moderate enlargement of the abdominal and retroperitoneal lymph nodes. The liver weighed 650 gm. and was moderately congested. The biliary tree, gastrointestinal tract, and pancreas were normal. Except for congestion, the adrenals, kidneys, ureters, and urinary bladder were unchanged. Genitalia were male and infantile. Examination of the calvarium and its contents revealed moderate edema and congestion of these tissues only.

Microscopic sections of the neoplasm (Fig. 1) revealed an extremely loose reticular fibrous stroma diffusely permeated by small basophilic cells with scanty cytoplasm and of lymphocytic character. Scattered nuclei were hyperchromic, while an occasional cell was in mitosis. In some areas, an occasional cell of relatively large size with a slightly acidophilic cytoplasm was noted. These cells had ovoid vesicular nuclei and prominent nucleoli characteristic of thymic epithelial cells. Such neoplasm was confined to the mediastinum and contiguous structures.

Final diagnosis of malignant thymoma, lymphocytic type, with extension to involve the contiguous structures including pericardium, diaphragm, pleura, hilus of each lung, and structures of base of neck was submitted.

Case 2. J.E.S., a 13-year-old white female, was admitted to the Lincoln General Hospital (No. 26684) on Jan. 4, 1961. She had been in good health until a month ago when she complained of pain and weakness in the left shoulder area, pains in her left ear, and vertigo. When the complaints persisted in spite of symptomatic therapy, further diagnostic measures were employed, including an X-ray film of the chest. This revealed left pleural effusion with displacement of the heart and mediastinum to the right and the presence of a large anterior mediastinal tumor. Hospitalization was advised for further evaluation and therapy.

No history of past illness was obtained. Tonsillectomy and adenoidectomy were performed on Jan. 30, 1957, because of nasal obstruction and hearing loss, pronounced during periods of upper respiratory infection. General development had been normal.

On examination at the time of hospital admission, she appeared to be well developed and nourished and in no apparent distress. Her temperature was 99.6° F., respirations were 24 per minute, and pulse was 96 per minute. No abnormality of the ears, eyes, or nose was detected. The mucosa of the oral pharynx was injected, and a small area of ulceration of the mucosa of the palate was seen. A number of small cervical lymph nodes were palpable. A systolic murmur was detected over the precordium. Although changes were not detected on percussion, increased breath sounds and vocal fremitus were found over the upper segment of the left thorax. No abnormalities of the abdomen were noted. The hemoglobin was 12.2 gm. per 100 ml., red cell count 4,150,000 per cubic millimeter, and white cell count 10,000 per cubic millimeter with 74% segmented neutrophils, 3% staff neutrophils, 2% eosinophils, 17% lymphocytes, and 4% monocytes. A urinalysis was normal.

Biopsy of left supraclavicular lymph nodes was performed on Jan. 5, 1961. Only a mild hyperplasia was found on microscopic evaluation of several small lymph nodes excised from this area. Thoracentesis on the left was accomplished on Jan. 9, 1961, with aspiration of 620 ml. of slightly bloody turbid fluid. Smear and cell block

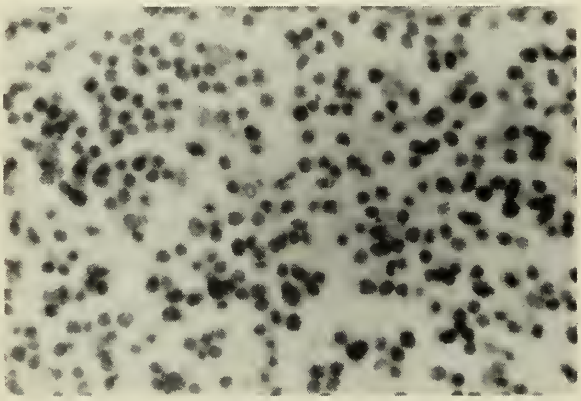

Fig. 1. Case 1

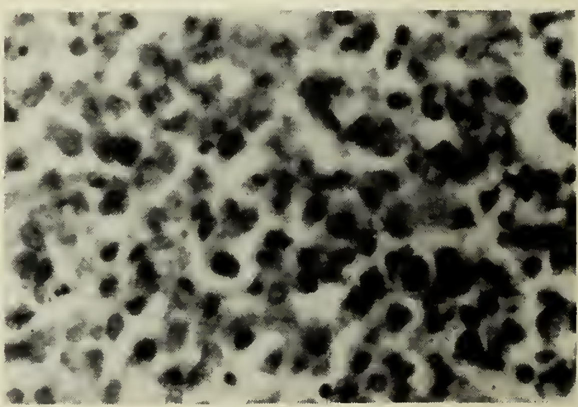

Fig. 2. Case 2

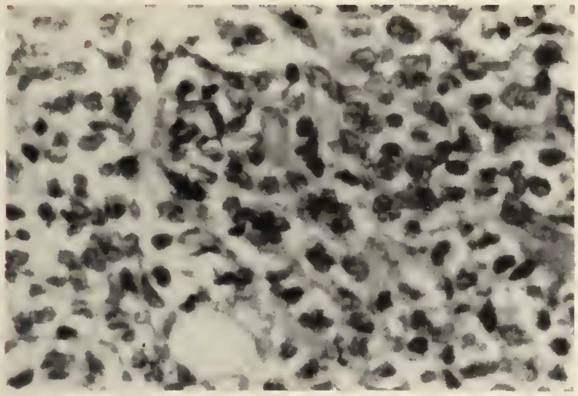

Fig. 3. Case 3

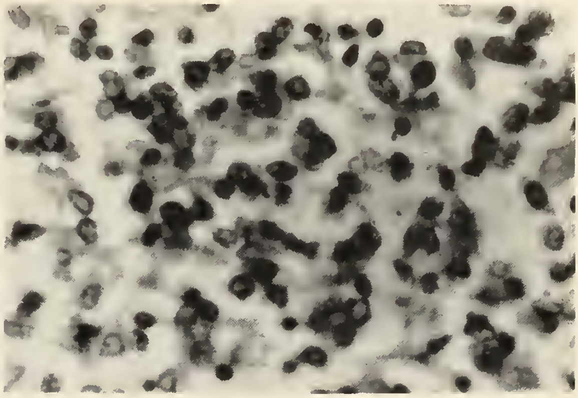

Fig. 4. Case 3

preparations of the sediment (Fig. 2) revealed the presence of masses of neoplastic cells along with scattered neutrophils and red blood cells. The majority of the cells had scanty cytoplasm with small basophilic nuclei characteristic of lymphocytes. In addition, large numbers of cells with eosinophilic cytoplasm and large ovoid vesicular nuclei and prominent nucleoli were seen. A few binucleated cells were noted as well as numerous cells in mitosis. Although cytology was suggestive of thymic epithelial and lymphocytic cells derived from malignant thymoma, malignant lymphoma could not be excluded.

Following irradiation therapy to the anterior and left lateral thorax, the hydrothorax cleared and there was a marked reduction in the size of the tumor mass. Subsequent to completion of the course of X-ray therapy on Feb. 7, 1961, there was continued improvement in her physical status. On readmission to the hospital on June 12, 1962, for psychiatric therapy necessitated by the emotional trauma which she experienced from her previous illness, no active organic disease process was detected. She expired suddenly and unexpectedly at home on June 25, 1962. An autopsy was not performed.

Case 3. J. C. S., a 3-year-old male, was admitted to the Lincoln General Hospital (No. 39722) on June 12, 1962, because of fever, irritability, listlessness, and a cough of approximately ten days' duration. He had been seen in the office on June 4, 1962, for treatment of an acute nasopharyngitis and tonsillitis. Although the acute symptoms had subsided following therapy, decreased breath sounds were noted over the entire left lung field. X-ray revealed opacity of the hilar and middle third of the left lung.

The child had been delivered at this hospital on June 14, 1959, with birth weight of 8 lb. 14 oz. He had the routine inoculations. Although there had been no previous hospitalization, he had received treatment for a celiac syndrome over the last two years.

On examination at the time of hospital admission, his temperature was 101.4° F., and there was evident respiratory distress. The mucous membranes of the nose, nasopharynx, and tonsillar regions were injected. Bilateral submaxillary lymphadenopathy was present. The thoracic movements were symmetrical with a lag on the left. Decreased breath sounds and dullness to percussion were noted over the lung fields, most pronounced on the left. The trachea was deviated to the right. No masses were palpable nor tenderness elicited on examination of the abdomen. Genitalia were male and infantile. The hemoglobin was 12.9 gm. per 100 ml., red cell count 4,510,000 per cubic millimeter, and white cell count 12,450 per cubic millimeter with 60% segmented neutrophils, 1% staff neutrophils, 1% eosinophils, 35% lymphocytes, and 3% monocytes.

Further X-ray studies confirmed the presence of a large, up to 5-cm. in diameter mass in the left paramediastinal area with shift of the mediastinum to the right. There was also elevation of the left leaf of the diaphragm suggesting involvement of the phrenic nerve. A right anterior scalene lymph node biopsy revealed only a mild, nonspecific hyperplastic lymphadenitis. Following preliminary irradiation therapy to the mediastinal mass, exploratory thoracotomy was performed June 27, 1962. A large, firm, somewhat lobulated tumor was found in the anterior mediastinum with extension to the upper reaches of the left pleural cavity as well as into the right thoracic cavity. Such extension of tumor precluded surgical excision, and the chest was closed after obtaining a biopsy of the tumor. The tumor (Fig. 3) consisted of myriads of small basophilic cells of lymphocytic type in a lobular arrangement. In some areas, sheets of larger cells with a more vesicular nuclear pattern were encountered, along with considerable mitotic activity characteristic of a lymphoblastic component. A few large reticuloendothelial or thymic epithelial cells were also detected. The tumor was classified as a malignant thymoma of the lymphocytic type. Although there was good response to subsequent irradiation therapy, progression of the disease was evident. He was readmitted to the hospital on June 9, 1963, and died June 11.

At autopsy, the body was that of a well-developed and fairly well-nourished male. Size and weight were considered within normal limits for his age. A large, 6-cm. long by up to 4-cm. in diameter neoplasm was present within the peritoneal cavity incorporating loops of bowel and extended from the under surface of the liver down to the region of the cecum. The mass was intimately associated with the capsule of the liver and appeared to infiltrate the adjacent hepatic parenchyma, but no additional tumor nodules were found within the substance of the liver. The tumor had produced obstruction of a loop of small bowel with resultant perforation and diffuse acute peritonitis. Although considerable gray-white fibrous tissue containing residual tumor was present throughout the mediastinum and there was marked thickening of the pleura and pericardium with similar tissue, the large, lobulated, neoplastic mass was no longer evident. Large, up to 2.5-cm. in diameter lymph nodes partially surrounded the aorta, esophagus, and trachea. There was similar lymph node enlargement throughout the abdomen and retroperitoneum. Multiple sections of the neoplasm (Fig. 4) and lymph nodes revealed sheets and strands of large, lymphoblastic cells along with numerous lymphocytic cells of a more mature character. The pattern was rather uniform throughout, although varying amounts of a fibrous stroma were encountered. In some areas, zones of necrosis of the tumor were prominent. The histopathology was that of a malignant lymphoma of the lymphoblastic lymphosarcoma type.

DISCUSSION

This family, with deaths in three of five siblings from malignant lymphoma, represents one of the rare types of familial involvement, heretofore infrequently reported.[27] More often, several generations have been involved, rather than a single generation. The time span of a fourteen-year period during which new cases of lymphoma appeared, however, is quite typical of the one- to three-decade interval which often elapses from the first observed to the most recent case onset in many families. Different physicians have often taken care of successive cases, in part due to family migrations especially in urban areas. When there is knowledge of the occurrence of previous lymphoma, as in this family, the index of suspicion may be higher for similar diseases in other relatives, and diagnosis may be more rapidly achieved.

A number of unsettling and presently unsolved questions evolve from this investigation. In these three siblings with similar childhood lymphomas, what are the common genetic or environmental circumstances related to their illness? As in the so-called "clusters" (families or communities), why did two siblings and many other persons at risk remain unaffected? Why are these illnesses so similar, and did the thymic involvement, present in all cases, affect the onset or outcome? What kind of microbiologic agent could be held responsible for a role in these illnesses?

The genetic background may be pertinent to the occurrence of malignant lymphoma in three of the siblings, since only the three with antecedent cutaneous melanotic pigmentation acquired the disease. This physical finding was present in a number of maternal relatives. According to the parent's observation, both of the initial patients, R. W. S. and J. E. S., were born with large, nonelevated brownish spots on the trunk or legs. The next two siblings, who are still well at the present time (C. S., aged 16, and K. S., aged 9), have no such pigmentation. The youngest sibling with malignant lymphoma, J. S., had what appeared to be a typical café au lait pigmentation on his left lateral thorax, present since birth. There were no stigmata suggestive of neurofibromatosis on any of the siblings and no other recognized congenital anomalies.

The possible characteristics of a viral or PPLO-type agent which could possibly be responsible, at least in part, for the induction of malignant lymphoma over an extended time period in this family are several.[28,29] It would require a susceptible host in terms of the acceptance of the particle by the host cell. The "fit" of the virus and the host deoxyribonucleic acid (DNA) or ribonucleic acid (RNA), to result in ultimate malignancy, must be genetically determined. Subsequently, either latent or smoldering malignant change, possibly including viral nucleic acid "capture," must occur. In addition, some form of "tolerance" must be acquired by the host if the virus or "new" cell is antigenically foreign in order for it to survive.

The agent might, therefore, have a relatively long incubation time from cell penetration to overt disease, as has been seen in certain animal disorders. The agent might cohabit an animal or other biological vector as a means of sustaining infectivity over many years.[20] It is also possible that vertical transmission from mother to fetus of either virus or cells containing or altered by virus could initiate disease.[30,31]

Perhaps the most striking feature of this family was the occurrence of morphologically similar tumors arising from the lymphoid system, with involvement of the thymus in all. Common to these three cases is a neoplasm arising in the thymic region. The principal cell type involved in the neoplastic processes is the lymphocyte, the principal component of the normal thymus gland. Consequently, one may postulate that the neoplasm in each of the cases represents a type of lymphoma. In none of the cases was myasthenia gravis a consideration.

It is not the purpose of this paper to become involved in the controversial interpretation of thymic lesions but rather to present three siblings with a lymphoproliferative malignancy. In Cases 1 and 2, the lesions were localized and arose in the anterior mediastinum but extended and infiltrated the contiguous structures of the mediastinum and the pleura without evidence of metastases via the bloodstream or lymphatics. On the basis of the cell type and following the classification proposed by Lattes,[32] these tumors are classified as thymomas of predominately lymphoid type. As death of both patients is attributed to the neoplasm, the process was certainly malignant in its behavior.

The neoplasm in Case 3, although originating in the anterior mediastinum, involved the lymphatics of the thorax as well as the abdomen and retroperitoneum. Such behavior, while not seen with a thymoma,[33] is characteristic of a malignant lymphoma. The original biopsy, considered adequate to establish a tumor of thymic origin, suggests a malignant lymphoma arising within thymic tissue rather than within mediastinal lymph nodes. Residual, uninvolved thymic tissue was not detected at autopsy. The distribution of the tumor and its morphologic characteristics confirm the opinion of a malignant lymphoma.

Thymic involvement by malignant lymphoma offers a two-fold possibility for speculation. If immune function is compromised, either during early life or later, then a tolerant state could explain the acceptance of an otherwise rejectable virus-like agent. On the other hand, lymphocytic mutation of a malignant type could begin in the thymus (from x cause) and give rise to clinical lymphoma.[34] Schwartz has recently shown that animals given "runt" disease ultimately develop a lymphoma-type illness.[35] The removal of the thymus in the newborn results in a higher susceptibility to viral oncogenesis and, in fact, this can be related also to genetic factors in mice.[36,37] Thus, the thymus could play a dual role in the onset and acceleration of this malignancy.

The majority of familially occurring neoplasms of the hemopoietic system reported in the literature arise from the lymphatic system.[38] From our own experience, based upon a survey of all hemopoietic and lymphatic neoplasms occurring in a five-year period in a population of about 110,000 living in six counties in southcentral Nebraska, this is also true. Bovine and porcine leukoses, which are the most common malignant tumors of large domestic animals after bovine "cancer-eye," are of lymphoid origin and are indistinguishable histologically from human chronic lymphatic leukemia and lymphosarcoma.[39] The laboratory mouse, various strains of which harbor one or more oncogenic viruses, is characterized by a relative lymphocytosis which precedes any manifestation of leukemia or the multiple tumor induction by polyoma virus. In this respect, the cow is similar, since absolute and relative lymphocytosis is accepted by most observers as an indication of herd infection with the agent of bovine leukosis and presages clinical lymphatic leukemia or lymphosarcoma within three to five years of onset.[39–41]

Several reports deny any familial tendency for multiple cases of acute childhood leukemia, which was suggested as a possibility by the family reported by Anderson, in which five out of eight siblings died within a four-year period with acute leukemia.[27] Radiation-induced leukemia thus far has often been myelogenous in nature. Except for a few recent episodes of an increased quantity of I^{131} from nuclear weapon fallout, whole-body radiation environmental sources in eastern Nebraska are small, since 50 to 100 ft. of loess covers the bedrocks.

The rural background and farming occupation of this family for several generations are similar to the environment and occupation characteristics of the other multiple family cases which have been recorded in Nebraska. Those concerned with leukemia and lymphoma patients may now recognize the similarity of these neoplasms, in frequency of occurrence and pathologic features, to malignant lymphoproliferative and myeloproliferative diseases of pets and of domestic animals living in close symbiosis with man. Not only do many patients intimately share in chronic exposure to the microbiologic flora of dogs and cats in the home or to that of pigs, chickens, and cattle on the farm, but nonsterile dairy supplies and eggs are distributed and consumed by most urban dwellers.

The farm upon which the siblings grew up was a mixed operation including one or more dairy cows from which the family consumed raw milk. The youngest sibling, J. S., was noted to develop a foul, slimy diarrhea when he was transferred from breast feeding to cows' milk at the age of 6 months. This consumption thereupon ceased. Over 90% of other families whom we have interviewed, including control observations, give a history of raw milk consumption from their own dairy cattle for many previous years. Many of these dairy cattle are derived from those introduced from Minnesota or Wisconsin according to local veterinarians. Bovine leukosis has recently been identified as a frequent enzootic disease in every county in Minnesota.[39] The parents of this family recalled no disease resembling leukosis in their domestic animals, except in occasional home-butchered diseased chickens.

There was ample contact with a wide variety of domestic animals and pets for many years in this family, so an exchange could take place with any agent capable of species cross infection. Of course, the presence of chemicals and other physical and environmental hazards is likely to be similar in this family.

The occurrence of carcinoma of the cervix in the mother of this family at the age of 42 recalls the observation of Videbaek concerning the somewhat higher incidence of carcinomas and other types of sarcoma in the blood relatives of leukemia and lymphoma patients[42] (see Fig. 5). The occurrence of an Ewing's sarcoma in a paternal cousin is also documented. These were the only known malignancies in the relatives, but the siblings of the parents are still rather young in mean age, so it is not yet possible to establish the ultimate occurrence of carcinoma

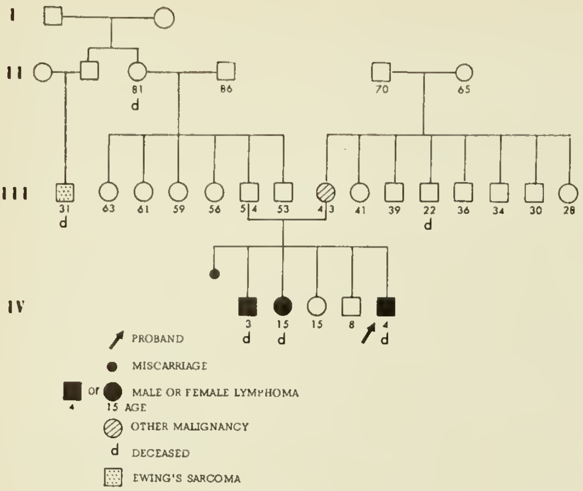

Fig. 5

in the first generation antecedent to the patients in this study. Excessive cancer deaths in relatives of leukemic and lymphomatous patients compared to the population in general have been both confirmed and denied by other studies.

SUMMARY

The occurrence of remarkably similar malignant lymphomas is reported in three siblings, occurring over a fourteen-year period. Hereditary and environmental factors in this family are discussed with regard to etiologic considerations currently under investigation.

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Rectal Mucosal Biopsies as a Diagnostic Aid in Cystic Fibrosis

I. H. JABRO, M.D., and G. E. GIBBS, M.D.
Omaha

CYSTIC FIBROSIS involves many organs including bronchi, pancreas, liver, salivary glands, labial mucus glands, Brunner's glands, and rectal mucus glands. The most satisfactory clinical method of diagnosis at present is determination of sodium and chloride in sweat. Curiously, the sweat gland shows no histological abnormality by light microscopy. Some cytoplasmic nodules, described from electron microscopy in cystic fibrosis, suspected of being mucoid have been described but this observation has not yet been confirmed.[1]

There is great variability in the degree to which various organs are involved in cystic fibrosis. Survival depends mainly on the pulmonary lesion. Before availability of the sweat test, diagnosis was confirmed principally by duodenal aspiration, with determination of pancreatic trypsin. Variability in the involvement of the pancreas is demonstrated by the fact that approximately 10% of the cases of cystic fibrosis show incomplete pancreatic exocrine deficiency.[2] An occasional case of cystic fibrosis shows normal sodium chloride concentration in the sweat. Many more show levels close to the borderline range. The degree of manifestation of various abnormalities in cystic fibrosis is not necessarily parallel in different organs in the same patient. Thus, pancreatic deficiency may be complete while pulmonary manifestations are minimal. Pulmonary manifestations may be fatal at an early age while pancreatic deficiency is only partial. It is, therefore, useful to have other criteria which may, on occasion, be definitely diagnostic of cystic fibrosis at times when usual criteria are negative or borderline. One such criterion, recently described, is the histological appearance of labial mucus glands as obtained by biopsy.[3]

METHODS AND MATERIALS

The present study concerns diagnostic use of the rectal mucosal suction biopsy. This has been reported by Rubin with various collaborators.[4,5] Parkins and associates[6] presented studies of 11 patients with sweat chloride concentrations above 80 mEq. per liter in which interpretation of rectal suction biopsy indicated cystic fibrosis definitely in 7, questionably in 2, and failed to indicate it in 2. In microscopic sections, the criteria were crypt dilatation, widening of the crypt wall due to abnormally tall goblet cells, gaping of the crypt mouth, sometimes with mucus being extruded, and very prominent goblet cells which seem to crowd out the intervening columnar cells. Enlargement or dilatation of the crypts tended to make the crypt width larger compared to the width of the intervening lamina propria. In the rectal mucosal biopsy, coarseness of the mucus gland crypts in cystic fibrosis was observed grossly with a hand lens. In the latest presentation by Rubin and his associates,[7] a further attempt was made to evaluate the reliability of the method. Blind interpretation of the slides was made by 3 observers in 139 biopsies taken from 74 cystic fibrosis patients; 72% were read as positive, 22% negative, and 6% questionable. Of 74 control specimens, 6 were falsely read positive, 60 negative, and 8 questionable. The principal criterion was dilatation of the crypts. The above study appeared while our own observations were in progress.

In our series, 59 rectal suction biopsies were taken, 30 from 27 subjects without cystic fibrosis and 29 from 24 patients with cystic fibrosis. Ages in the controls ranged from 1 month to 11 years. Ages in the cystic fibrosis patients ranged from 6 months to 19 years.

The instrument used was the multipurpose tube of 4.6 mm.-diameter. The metal capsule, of

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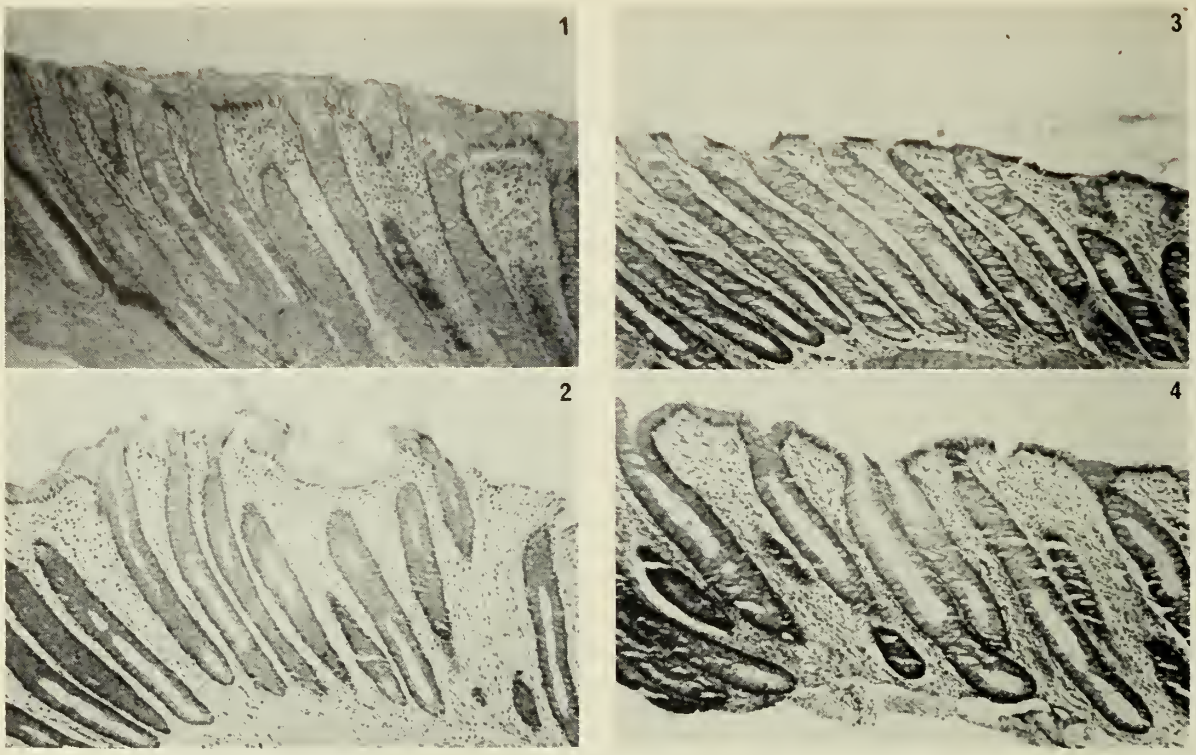
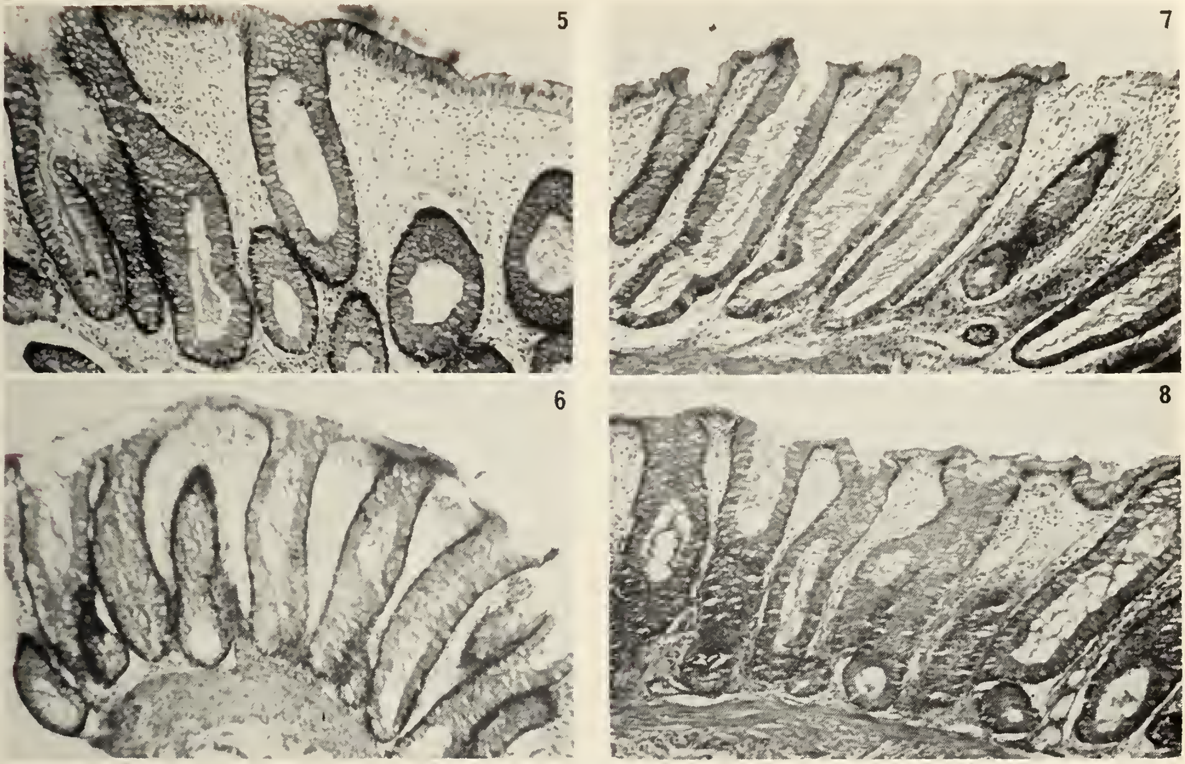
I. H. JABRO *is a resident and Cystic Fibrosis Fellow of the National Cystic Fibrosis Research Foundation, and* G. E. GIBBS *is professor and chairman, Department of Pediatrics, University of Nebraska College of Medicine, Omaha.*



Figs. 1-4. Microphotographs of biopsies from control children show the following characteristics: [1] narrow glands, [2] no gaping of the gland opening, [3] no cryptic dilatation, [4] moderate amount of mucus, and [5] no distortion of the configuration of the glands.

approximately the same diameter, has a 2.9-mm. aperture behind which slides a circular knife controlled by a steel wire. (The biopsy tube is obtainable from W. E. Quinton and Company, Seattle, Wash.) The tube was passed into the anus approximately 5 cm. to bypass the confusing morphology of the anal region, but not so far as to reach the region of the bowel which is free in the peritoneal cavity. The tube was introduced with the knife closed, the wire was then advanced to open the capsule aperture, and a small amount of air was injected to insure patency of the tube. A negative pressure was applied by means of the syringe and controlled by a manometer. This negative pressure ranged from 4 to 10 in. of mercury, according to the age of the subject. After application of this suction the biopsy specimen, protruding into the aperture of the capsule, was amputated by the knife, pulled by the steel wire. A successful biopsy could usually be detected by the "feel" as the operator pulled the wire. In order to obtain an additional specimen, the instrument could be moved for approximately a centimeter, the knife again pushed to open the aperture, the suction applied, and the knife pulled. After the tube was removed from the rectum, the capsule aperture was opened by pushing the knife distally. The capsule was cupped loosely in the hand and the biopsy specimens were blown out into the operator's palm by a forceful current of air from the syringe. The biopsy was then placed with the cut surface up on the end of a dry fingertip so that the cut surface could be placed down on a piece of filter paper or monofilament plastic mesh. The specimen was then imbedded in paraffin. Extreme care was taken in orientation of the tissue in the paraffin block in order to have cut sections exactly perpendicular to the mucosal surface. In some instances, the fixative was 10% formalin. The preferred fixative, however, was a phosphomolybdic acid fixative consisting of 20 ml. of 25% phosphomolybdic acid in 6.25 normal hydrochloric acid, 65 ml. of 95% ethyl alcohol, 10 ml. of 40% formalin, and 5 ml. of distilled water. This solution was freshly prepared just before use. Orientation of the specimen for cutting was a very important point because, if the sections were not cut at right angles to the lumen, the whole lengths of the glands did not show and interpretation was difficult. The entire specimen usually was sectioned serially. Only a few sections from the central core actually were needed for interpretation, and, in routine practice, only these need be saved. The sections were stained with periodic



Figs. 5-8. Microphotographs of biopsies from cystic fibrosis patients show the following characteristics: [1] wide glands [2] gaping of the gland opening, [3] wide dilatation of mucus glands, [4] large amount of mucus, [5] distortion of the configuration of the glands, and [6] prominent goblet cells.

acid–Schiff and hematoxylin-eosin. Some were stained with mucicarmine. The criteria mainly used in evaluation to indicate cystic fibrosis were: [1] wide dilatation of mucus glands, [2] gaping of the gland opening, [3] large amounts of mucus, [4] distortion of the configuration of the glands, [5] very prominent goblet cells, and [6] in several cases of cystic fibrosis, bifid mucus glands.

RESULTS AND DISCUSSION

Evaluation of the biopsies by independent observers, unaware of the diagnosis, resulted in 16 correct diagnoses of cystic fibrosis, 6 doubtful, and 1 false-negative. Similarly, evaluation of noncystic fibrosis cases gave a false impression of cystic fibrosis in 1, questionable in 5, and negative in 22. Microphotographs of 4 biopsies from 4 controls are shown in Figs. 1 through 4 and of 4 biopsies from patients with cystic fibrosis are shown in Figs. 5 through 8. Our own observations and those of Rubin and his associates indicated that, as a diagnostic method, the rectal biopsy is somewhat less definitive than the sweat test. It also may be somewhat less definite than labial mucus gland biopsy. It does, however, have certain advantages. There are probably cases in which the rectal biopsy is definite when the sweat test is equivocal. The rectal biopsy is convenient and painless.

In our own experience and in that of Rubin and associates there is a small proportion of patients who may have some bleeding which may be alarming, although it has never been serious. In one instance, the child was taken several hundred miles immediately after the biopsy. The family had been told that a small amount of bleeding might occur but not to be alarmed. After arriving home six hours later, they telephoned that there had been repeated passages of bright red blood and the child seemed to the parents to be pale and lethargic. The child was then taken to the local hospital where proctoscopic examination revealed no blood. As noted by Parkins and co-workers, occasional major bleeding episodes should be anticipated when any large series of rectal biopsies is undertaken. We resorted to local fulguration in one instance, but, even in this instance, there was no evidence of anemia. Care should be taken that there is not a defect of blood coagulation such as the hypoprothrombinemia which occasionally occurs in cystic fibrosis or celiac disease due to failure of absorption of vitamin K.

The histological observation of abnormality of rectal mucus glands in cystic fibrosis shows that the mucus abnormality of cystic fibrosis is present in this location and that this mucus, which may be conveniently and painlessly obtained free of contamination by purulent exudate or other secretions, may be a useful source of mucus for further studies of a mucus abnormality in cystic fibrosis.

SUMMARY

Rectal mucosal suction biopsies in 24 infants and children with cystic fibrosis and 27 infants and children without cystic fibrosis demonstrated this technique to be significantly diagnostic in a high percentage of cases. It is believed that this technique which is convenient, painless, safe, and practical is a useful addition to the diagnostic armamentarium in cystic fibrosis.

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Book Reviews . . .

External Otitis: Diagnosis and Treatment

by EDLEY H. JONES, M.D., *245 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $9.50*

This monograph by Dr. Edley H. Jones represents a tremendous amount of work and experience. The text makes a complete survey of the subject. In the first section basic anatomy is discussed, as well as the normal microanatomy and physiology of the skin of the external auditory canal. In part two, the author discusses his investigations on the pH reaction of the skin, the bactericidal effect of weak solution of acetic acid, and the normal bacteria flora of the external auditory canal. The microscopic pathology of various cases of external otitis, along with case reports, are recorded.

Later sections of the book discuss clinical diagnosis and treatment. The author includes history-taking, necessary equipment, various medications to relieve pain, and the treatment of the infection. He also discusses in detail the various types of otitis externa, their diagnosis and treatment.

All in all, this is a complete report on the subject, replete with illustrations, case reports, and treatment.

The illustrations, color plates, and text are excellent. This is recommended as an up-to-date reference volume on the subject.

DAVID MYERS, M.D.
Philadelphia

Therapeutic Radiology: Rationale, Technique, Results

by WILLIAM T. MOSS, M.D., *2nd ed., 524 pp., ill., C. V. Mosby Co., St. Louis, 1965. $18.75*

This book serves as an introduction to the subject of therapeutic radiology and deals with selected clinical problems most commonly faced in this field. It constitutes an excellent introductory text for any clinician or radiologist interested or involved in therapeutic radiology.

The book is divided into twenty-one chapters covering various organs and organ systems most commonly treated by radiology. The first chapter presents an introduction to general concepts of radiation therapy and the relationships of the radiation therapist to other medical specialists. An excellent section on radiation biology and dose-time relationships is also included here, as well as up-to-date information on the effects of increased oxygen tension on radiosensitivity.

The diagrams are for the most part informative and easily understood and the illustrations are of good quality. A current, complete bibliography is presented at the end of each chapter. The first part of each chapter discusses the radiation response of the particular organ when it is healthy. Information of this type is especially helpful, since frequently the radiation reaction in normal tissues is the controlling factor in therapy and these reactions must be properly understood.

Only a limited amount of information is presented on the treatment of benign conditions which, in this era of radiation therapy, is appropriate. More diagrams and illustrations showing treatment techniques and field arrangements would have improved the book, particularly for those beginning in radiation therapy. However, this purpose is probably best served by each individual training program.

The content of the book is factual and understandable. The author's views are those most generally accepted. I would recommend this book for anyone interested or involved in radiation therapy, especially the resident in radiology.

ROBERT J. OLSON, M.D.
Williston, North Dakota

Viral and Rickettsial Infections of Man

edited by FRANK L. HORSFALL, JR., M.D., *and* IGOR TAMM, M.D., *4th ed., 1,282 pp., ill., J. B. Lippincott Co., Philadelphia, 1965. $15.50*

There are few textbooks which serve in such excellent fashion the needs of both the clinician and the basic scientist. The evolution of simplified laboratory techniques for the facile isolation and study of viruses provides information of tremendous importance for both the investigator and the practicing physician.

The fourth edition of this text, given birth originally in 1940 by the late Thomas Milton Rivers, brings into sharp and very current focus the tremendous yield of two decades of productive basic research and lucid clinical observation. Some 57 experts summarize the fruits of their labors and those of others in crisp and thoughtful manner. The two most able editors, Frank L. Horsfall, Jr., and Igor Tamm, organize 54 chapters and an appendix on basic laboratory methods in such an artful way that the fundamental interests of clinicians and scientists, which might be considered in some quarters as rather disparate in nature, may be accurately and thoroughly fulfilled.

The historian, taxonomist, biophysisist, biochemist, biologist, geneticist, pathologist, epidemiologist, and indeed the chemotherapist of the future will find elegant recapitulation of their especial domain delineated in the initial sixteen chapters of the text. The investigator and the technologist struggling to acquire the laboratory skills of modern virology and rickettsiology will find solace and guidance in the appendix of the text which describes basic techniques in considerable detail. The clinician will find the text of significant aid as a ready and complete reference for the most recent concepts of human viral infections and the plethora of fancifully named pathogens which evoke them. Human illness defined in the past in anatomical and pathological terms may now be redefined and more fully appreciated in the light of viruses newly isolated and characterized, as well as old foes which have finally been captured in the test tube and so more accurately scrutinized. More clinically oriented chapters, numbering 38, delve into the biology of the virus (or Rickettsia), historical aspects, and a full treatise of the pathogenesis and pathology of the infection, clinical features, diagnosis (differential clinical and laboratory), treatment, epidemiology, and disease control. These

(Continued on page 10A)

(Continued from page 9A)

chapters are superb sources of information for thorough and current review of specific virus and rickettsial infections of man.

This text is incomparable and so extremely valuable and complete that it should be found in the personal library of every physician, medical scientist, and educator.

JOSEPH W. ST. GEME, JR., M.D.
Torrance, California

NEW BOOKS RECEIVED

Advances in Biology of Skin, Vol. VI: Aging, edited by WILLIAM MONTAGNA, 273 pp., ill., Pergamon Press, New York, 1965. $15

Aspects of Alcoholism, Vol. 2, preface by RUTH FOX, M.D., 80 pp., ill., J. B. Lippincott Co., Philadelphia, 1966. $3.50

Biochemical Approaches to Cancer by ERIC REID, D.SC., 198 pp., ill., Pergamon Press, New York, 1965. $3.95

The Ciba Collection of Medical Illustrations, Vol. 4: Endocrine System and Selected Metabolic Diseases, prepared by FRANK H. NETTER, M.D., guest editor, PETER H. FORSHAM, M.D., 287 pp., ill., commissioned and published by CIBA, 1965.

The Circulatory Response to Muscular Exercise in Man by ARNE CARLSTEN, M.D., and GUNNAR GRIMBY, M.D., 129 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $6.50

Congestive Heart Failure by RAYMOND T. BENACK, M.D., 117 pp., Charles C Thomas, Springfield, Ill., 1966. $5.50

A Current Technique of Aortoiliac and Femoropopliteal Endarterectomy for Obliterative Atherosclerosis by JACK A. CANNON, M.D., 54 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $4.75

Drugs of Choice 1966-1967, edited by WALTER MODELL, M.D., 969 pp., ill., C. V. Mosby Co., St. Louis, 1966. $16.75

Examination of Urine (A Programmed Text and Reference Book) by JOHN M. WELLER, M.D., and JAMES A. GREENE, JR., M.D., ill., plus filmstrips and viewer, Appleton-Century-Crofts, New York, 1966. $8.50 per set

Fundamental Considerations in Anesthesia by CHARLES L. BURSTEIN, M.D., 3rd ed., 223 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $8.50

Gonadotropins: Physiocochemical and Immunological Properties (Ciba Foundation Study Group No. 22), edited by G. E. W. WOLSTENHOLME and JULIE KNIGHT, 125 pp., ill., Little, Brown and Co., Boston, 1965. $3.50

Laboratory Experience in Psychology: A First Term's Work by B. BABINGTON SMITH, 240 pp., ill., Pergamon Press, New York, 1965. $4.50

Lung Circulation, Vol. I: Physiology and Pharmacology, and Vol. II: Pathologic Physiology and Therapy of Diseases by DOMINGO M. AVIADO, ill., Pergamon Press, New York, 1965. $50 per set

Managing your Coronary by WILLIAM A. BRAMS, M.D., 3rd ed., 175 pp., J. B. Lippincott Co., Philadelphia, 1966. $3.75

Man and Africa: A Ciba Foundation Symposium, edited by GORDON WOLSTENHOLME and MAEVE O'CONNOR, 400 pp., ill., Little, Brown and Co., Boston, 1965. $7.50

Medical Pharmacology: Principles and Concepts by ANDRES GOTH, M.D., 3rd ed., 668 pp., ill., C. V. Mosby Co., St. Louis, 1966. $12.50

The Neuroendocrine Control of Adaptation (International Series of Monographs in Pure and Applied Biology, Modern Trends in Physiological Sciences Division) by K. LISSAK and E. ENDRÖCZI, vol. 25, 180 pp., ill., Pergamon Press, New York, 1965. $11

Pediatric Therapy by HARRY C. SHIRKEY, M.D., 2nd ed., 1,223 pp., ill., C. V. Mosby Co., St. Louis, 1966. $18.50

The Peripheral Nervous System by J. P. SCHADE, 230 pp., ill., Elsevier Pub. Co., New York, 1966. $10

Principles of Pathology by HOWARD C. HOPPS, M.D., 2nd ed., 403 pp., ill., Appleton-Century-Crofts, New York, 1964.

Prognosis: A Guide to the Study and Practice of Clinical Medicine by LESLIE A. OSBORN, M.D., 286 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $10

Radiological Monitoring of the Environment, edited by B. C. GODBOLD and J. K. JONES, 425 pp., ill., Pergamon Press, 1965. $17.50

Rare Diseases in Internal Medicine by NEUTON S. STERN, M.D., 572 pp., Charles C Thomas, Springfield, Ill., 1966. $18.50

The Spiral After-Effect (International Series of Monographs in Experimental Psychology by HARRY C. HOLLAND, vol. 2, 128 pp., ill., Pergamon Press, New York, 1965. $6

Williams Obstetrics by NICHOLSON J. EASTMAN and LOUIS M. HELLMAN, 13th ed., 1,182 pp., ill., Appleton-Century-Crofts, New York, 1966. $18.75

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News Briefs . . .

North Dakota

DR. CHARLES R. TOMPKINS, an associate of the Tompkins and Countryman Clinic in Grafton, has been honored as a fifty-year member of the North Dakota State Medical Association. Dr. Tompkins received his medical degree from the Rush Medical College, Chicago, in 1916.

* * * *

DR. LELAND J. LARSON, a radiologist, has joined the Fargo Clinic staff. Dr. Larson had been in private practice in Minneapolis.

* * * *

DR. PERRY H. ENGSTROM, JR. of Wahpeton, a surgeon on the staff of the Wheaton Community Hospital, has returned from a tour of duty in Viet Nam.

* * * *

DR. MARIANNE WALLIS, a radiologist at St. Joseph's Hospital in Minot, has received the Sister Award as an outstanding woman of Italian descent. Dr. Wallis, who is originally from Vienna, Austria, was one of a group of women honored by Amita, Inc.

* * * *

DR. LOUIS B. SILVERMAN, a pediatrician at the Grand Forks Clinic, has been appointed chief of staff at Deaconess Hospital. Dr. Silverman is a member of the American Academy of Pediatrics.

* * * *

DR. JAMES R. AMOS of the North Dakota State Health Department, Bismarck, has been appointed medical advisor to the North Dakota State Employee Retirement Board.

* * * *

DR. GLENN W. TOOMEY of Devils Lake has been elected president of the North Dakota Medical Association. Dr. Verrill J. Fischer of Minot was named president-elect.

* * * *

DRS. BENNIE J. CLAYBURGH and JOHN J. MC LEOD, Grand Forks orthopedic surgeons, have opened the Orthopedic Clinic there. Both are members of the American Board of Orthopedic Surgery and the American Academy of Orthopedic Surgeons.

* * * *

DR. GEORGE L. COUNTRYMAN of Grafton has been elected president of the North Dakota Physicians Service at the group's annual meeting in Fargo. Other officers are Dr. Henry A. Norum, Fargo, vice-president; Dr. Wellington B. Huntley, Minot, secretary; and Dr. Amos R. Gilsdorf, Dickinson, treasurer.

* * * *

THE NORTH DAKOTA STATE MEDICAL ASSOCIATION held its 79th annual convention April 29-30 at Fargo, with the association's house of delegates holding meetings through May 1. Five doctors were honored for being fifty-year members of NDSMA. They are Dr. Angus L. Cameron, Minot; Dr. Max T. Lampert, Minot; Dr. Adam F. Panek, Milton; Dr. Paul H. Rowe, Minot; and Dr. Charles R. Tompkins, Grafton.

* * * *

DR. DOUGLAS R. DOSS, a radiologist at St. Luke's Hospital and Grand Forks Deaconess Hospital, will provide consulting radiology services for the Roseau Area Hospital.

* * * *

A SIX-COUNTY mental health out-patient clinic will open in Fargo this summer, according to Dr. Hale Aarnes, board president of the Southeast Region Mental Health and Retardation Association and professor of education at North Dakota State University. The Fargo region includes Cass, Ransom, Richland, Sargent, Steele, and Traill counties.

Minnesota

DR. MATTHEW J. WEIR, a Virginia specialist in internal medicine, is serving as a two-month volunteer physician in Viet Nam. Dr. Weir and other physicians are a part of Project Viet Nam, a program started by President Johnson to recruit U.S. doctors for short-term, volunteer service.

* * * *

DR. GEORGE M. MIKS, surgeon, is opening a new clinic in Eveleth. Dr. Miks comes from Oak Park, Ill., and received his medical degree from Marquette University School of Medicine, Milwaukee, in 1963.

* * * *

DR. CLAYTON A. JOHNSON, a native of Chisholm, is now with the U.S. Army in Viet Nam. Dr. Johnson received his medical degree from the University of Minnesota Medical School in 1964.

* * * *

DR. JEANETTE K. LOWRY of Minneapolis, a specialist in internal medicine, has been appointed to the Defense Advisory Commission on Women in the Services by Secretary of Defense Robert McNamara.

* * * *

DR. LOWELL L. HENDERSON, a Mayo Clinic allergist, has been elected president of the American College of Allergists. Dr. Henderson is also a member of the American Academy of Allergy.

* * * *

DR. DAVID S. BERKMAN, an internist at the Rochester State Hospital, announced plans to open a private practice at Emily.

* * * *

TEN MINNESOTA DOCTORS have received special citations for fifty years of medical practice from the Minnesota State Medical Association during the association's annual meeting in St. Paul, May 16-17. They are: Dr. Henry E. Binet, Grand Rapids; Dr. Bottolf T. Bottolfson, Moorhead; Dr. Austin C. Davis, Pompano Beach, Fla., formerly of Rochester; Dr. Thomas S. McClanahan, White Bear Lake; Dr. Samuel P. McDaniel, Lakeville; Dr. John A. McIntyre, Owatonna; Dr. Chauncey A. McKinlay, Minneapolis; Dr. John R. McNutt, Duluth; Dr. Joe M. Neal, Minneapolis; and Dr. Harry L. Smith of Rochester.

* * * *

DR. ROBERT W. SPLETTSTOESSER, an internist at Belle Plaine, has moved to Tracy and begun practice there.

* * * *

DR. EARL H. WOOD of the Mayo staff has received a $133,465 grant from the National Aeronautics and Space Administration for continuing aerospace research. Dr. Wood is an authority on aerospace medicine and will use the grant for further investigation on the effects of stress on the heart and lungs. He is currently studying in the Physiology Institute at the University of Berne, Switzerland, and will return this fall.

* * * *

DR. GRANT A. MASON, JR., an intern at Ohio State University Hospital, has been appointed to the Minnesota State Health Department to help plan and develop cancer education and control activities.

(Continued on page 14A)

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NEWS BRIEFS

(Continued from page 13A)

DR. CHARLES G. SHEPPARD of Hutchinson has been named president-elect by the Minnesota State Medical Association's House of Delegates at the organization's annual meeting May 17 in St. Paul. Dr. Sheppard will succeed current president Dr. Robert P. Buckley of Duluth Jan. 1. Others elected were Dr. Raymond J. Jackman, Rochester, first vice-president; Dr. Charles J. Beck, North St. Paul, second vice-president; Dr. Barnard Hall, St. Paul, secretary; Dr. Charles A. Neumeister, Minneapolis, treasurer; Dr. John T. Pewters, Minneapolis, speaker of the house; and Dr. Leon E. Steiner, Albert Lea, vice-speaker.

* * * *

DR. ARNOLD LARSON, retired Detroit Lakes general practitioner, has received a life membership in the Clay-Becker County Medical Society.

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DR. ROBERT R. KIERLAND, head of the section of dermatology at the Mayo Clinic, has been reelected secretary of the American Dermatological Association.

* * * *

DR. W. SPENCER PAYNE of the Mayo Clinic staff has been elected to the board of directors of the Minnesota Surgical Society.

* * * *

DR. JOHN P. UTZ, professor in the department of medicine of the Medical College of Virginia, Richmond, and formerly of Rochester, has received a medical research grant from Wyeth Laboratories. Dr. Utz is a specialist in fungus diseases.

* * * *

THE RURAL MEDICAL SCHOLARSHIP awarded annually to a freshman at the University of Minnesota Medical School by the Minnesota State Medical Association, was presented this year to Kenneth Heithoff, 22, of Verndale. Heithoff received his B.S. degree from St. Thomas College, St. Paul.

* * * *

THE ADMINISTRATION AND FACULTY will support an expansion of the University of Minnesota Medical School if the legislature provides sufficient funds, according to Dr. Robert B. Howard, dean of the school. A legislative subcommittee has begun a study into the feasibility of increasing the size of the entering class from the present 150 to 250 students. Preliminary findings by the Health Manpower Advisory Commission call for an entering class of 200 as "an immediate solution," with eventual expansion to 250 students. The commission, however, also recommends establishment of another four-year medical school.

* * * *

MOUNT SINAI HOSPITAL in Minneapolis has received $114,325 from the U. S. Public Health Service to establish a rehabilitation center for patients with emphysema or chronic bronchitis. The project is designed to demonstrate proper treatment and rehabilitation, including regimens of drug and inhalation therapy, breathing exercises, regular check-ups, home care, postural drainage, and physical conditioning.

* * * *

DR. ROBERT A. GOOD, professor of pediatrics and microbiology at the University of Minnesota, has received an honorary doctor of medicine degree from the University of Uppsala, Sweden, in recognition of outstanding research and educational efforts over the years. Dr. Good's research in the field of immunological investigations has produced evidence strongly supporting the fundamental role of the thymus gland in the development of immunity.

* * * *

DR. LEONARD W. GOLDMAN, a Minneapolis psychiatrist, will serve as a consultant for the Sioux-Trails Mental Health Center at New Ulm on a 1-day-a-week basis.

* * * *

DR. OWEN H. WANGENSTEEN, professor and chairman of the department of surgery at the University of Minnesota Medical School, has been elected to the National Academy of Sciences.

* * * *

AN INTERNATIONAL SYMPOSIUM on liver disease in honor of Dr. Cecil J. Watson, professor and head of medicine at the University of Minnesota College of Medical Sciences, was held at the University May 23-25. The three-day symposium featured speakers from the United States, Germany, England, and Canada. Dr. Watson is leaving the University July 1 after thirty-one years of teaching, research, and administration to head a new program in teaching and research at Northwestern Hospital in Minneapolis. He also will retain his position as a full professor at the university, specializing in liver diseases.

* * * *

DR. WILLIAM N. SPELLACY has received a $45,000 grant from the Josiah Macy, Jr. Foundation for use in education and research. Dr. Spellacy is a fellow in obstetrics and gynecology at the University of Minnesota and is conducting several research projects on metabolic changes in women.

* * * *

DR. RICHARD V. EBERT has been named head of the department of medicine in the University of Minnesota College of Medical Sciences. Dr. Ebert, now head of the department of medicine at the University of Arkansas Medical School, will succeed Dr. Cecil J. Watson on July 1. A graduate of the University of Chicago School of Medicine, Dr. Ebert is an authority on lung disease.

* * * *

THE SECOND ANNUAL SYMPOSIUM on kidney disease, sponsored by the Upper Midwest Chapter of the National Kidney Foundation, will be held Sept. 14, 1966, at the St. Paul Hilton Hotel. Dr. John M. Burns, Midway Medical Arts Building, St. Paul, is the chairman of the symposium.

* * * *

THE MINNEAPOLIS WAR MEMORIAL BLOOD BANK has installed equipment for processing frozen blood. Equipment consists of an ultra low temperature freezer for storing blood at −85° C. and a cytoglomerator for reconstituting the blood. This will enable the blood bank to store rare type bloods indefinitely, rather than the present 21 days. This is the first such unit installed west of the Mississippi River.

* * * *

DR. ARTHUR M. OLSEN, an internist on the Mayo Clinic staff, has been reelected president of the Minnesota Tuberculosis and Health Association.

* * * *

DR. ANDREW P. GOBLIRSCH was honored at the annual banquet of the Sleepy Eye Chamber of Commerce for

(Continued on page 16A)

'Pentetra'— 80 TDC

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(Continued from page 15A)

forty years of service to the community. Other physicians on the staff of the Sleepy Eye Municipal Hospital were also honored.

* * * *

DR. HILDEGARD K. GRABER, a psychiatrist, has left a post at Hastings State Hospital to enter private practice in St. Paul.

* * * *

DR. ELIZABETH K. RIESCHL of Jordan now is associated with the New Prague Medical Clinic on a part-time basis.

* * * *

DR. ELMER E. KEITHAHN, a general practitioner in Sleepy Eye for twenty-two years, has opened a new clinic there. He will be joined by Dr. Elton Wing, now an intern at Ramsey County Hospital in St. Paul.

* * * *

DR. JON D. WEMPNER, Lakeview Clinic, Waconia, has been elected to active membership in the American Academy of General Practice.

* * * *

DR. NEIL D. NICKERSON, a Fairmont internist, has been admitted to full fellowship in the American College of Physicians.

* * * *

THE AMERICAN ASSOCIATION FOR THE HISTORY OF MEDICINE held its 39th annual meeting May 11-14 in Rochester and Minneapolis. Nearly 200 academicians and students attended the lectures and exhibits.

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DR. MICHEL I. SABBAGH of McLaughlin has been elected to active membership in the American Academy of General Practice. Dr. Sabbagh received his medical degree from the University of Saint-Joseph, Beyrouth, Lebanon, in 1951.

* * * *

DR. PAUL G. BUNKER, an Aberdeen otolaryngologist, received the Chevalier Jackson award in San Juan, Puerto Rico, during the 46th annual convention of the American Broncho-Esophagological Association.

Deaths . . .

DR. NELLIE N. BARSNESS, 92, St. Paul general practitioner and surgeon, died May 12. A 1902 graduate of the University of Minnesota Medical School, Dr. Barsness attended the Vienna eye, ear, nose, and throat school, and did postgraduate work in eye surgery in Berlin, Germany. She served in the French army in World War I as an eye surgeon and was decorated by the French minister of war. Dr. Barsness conducted clinics at Nancy, France, and Rheims, Germany, and was a member of the 50-year club of the Minnesota State Medical Association and numerous other organizations.

* * * *

DR. GALEN H. ADKINS, 57, medical director of the Cambridge State School and Hospital at Cambridge, Minn., died April 27. Dr. Adkins was superintendent of the state mental hospital at Sandstone, Minn. from 1957 to 1959 and superintendent of the Cambridge hospital from 1959 until he became medical director in 1964. Dr. Adkins received his medical degree from the University of Minnesota Medical School in 1935.

* * * *

DR. ARNOLD E. HETZLER, 64, a general practitioner in Mandan, N. Dak. died May 12. Dr. Hetzler practiced medicine at Richardton before moving to Mandan in 1933. He received his degree from the University of Minnesota Medical School in 1929.

* * * *

DR. STEPHEN A. DONAHOE, 78, died in Sioux Falls May 1. Dr. Donahoe was a general practitioner in Sioux Falls for more than half a century. He received his medical degree from the University of Illinois College of Medicine in 1912.

* * * *

DR. CHARLES E. MERKERT, 69, of Minneapolis died May 18. Dr. Merkert had been chief of staff at Lutheran Deaconess Home and Hospital before his retirement and was active in several public health associations. He received his medical degree from the University of Minnesota in 1922.

* * * *

DR. CLAIR C. CRAIG, 89, an International Falls, Minn. pioneer doctor and civic leader, died May 15. Dr. Craig was a Minnesota native and practiced medicine in International Falls for almost fifty years. He received his medical degree from Indiana University School of Medicine in 1917.

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1 Sherman, L. F. Minnesota Med 48,605 May, 1965. 2 Sherman, L. F. Personal Communication.

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Description: CORTENEMA Hydrocortisone Retention Enema is a completely disposable, single-dose unit consisting of a flexible plastic container with a lubricated applicator tip for rectal administration. It is designed to permit self-administration and, therefore, it is suitable for both out-patient and hospital use. It also may be diluted with isotonic saline for administration by intrarectal drip.

CORTENEMA consists of a suspension of partially solubilized hydrocortisone alcohol in an aqueous vehicle. Thus, it provides the potent anti-inflammatory effect characteristic of the corticosteroids. Because hydrocortisone alcohol is absorbed to some extent from the colon, CORTENEMA provides both topical and systemic actions.

Indications: CORTENEMA Hydrocortisone Retention Enema is indicated as an adjunct in the treatment of idiopathic nonspecific ulcerative colitis. It is most useful in cases involving the rectum, sigmoid and left colon, where it exerts a topical effect. Due to its systemic action, CORTENEMA has proved effective in certain cases extending to the transverse and ascending colons.

Rectal steroid therapy brings about prompt symptomatic and proctologic remissions in a significant proportion of patients, but it apparently does not alter the recurrent and progressive nature of ulcerative colitis. Therefore, this form of treatment is not recommended for prophylaxis during periods of remission.

Contraindications: Local contraindications to the use of intrarectal steroids include obstruction, abscess, perforation, peritonitis, fresh intestinal anastomoses, extensive fistulas and sinus tracts. Tuberculosis (active, latent or questionably healed), ocular herpes simplex, and acute psychosis are usually considered absolute contraindications to the use of corticosteroids.

Relative contraindications include active peptic ulcer, acute glomerulonephritis, myasthenia gravis, osteoporosis, diverticulitis, thrombophlebitis, psychic disturbances, pregnancy, diabetes, hyperthyroidism, acute coronary disease, hypertension, limited cardiac reserve, and local or systemic infections, including fungal or exanthematous diseases. Where these conditions exist, the expected benefits from CORTENEMA must be weighed against the risks involved in its use.

If clinical or proctologic improvement does not occur within two or three weeks after starting CORTENEMA, discontinue its use.

Precautions: CORTENEMA Hydrocortisone Retention Enema should be administered with caution in patients with severe ulcerative disease because these patients are predisposed to perforation of the bowel wall. In the advanced stages of chronic ulcerative colitis, where there is loss of mucosa, and thickening and fibrosis of the bowel wall, steroid therapy theoretically might hasten deterioration, although this has not been proved with steroids in actual practice.

In severe cases, where surgery is imminent in the absence of marked clinical improvement, it is hazardous to wait more than a few days for a satisfactory response to medical treatment.

Because of the possibility of adrenal insufficiency caused by suppression of the adrenal cortex by glucocorticoids especially after prolonged therapy, it is important that therapy be withdrawn gradually. If the patient is subjected to unusual stress, while on therapy or up to a year after discontinuation of steroids, adequate supportive measures and increased or reinstated systemic steroid therapy are indicated. In the case of surgery, these measures should be continued throughout the pre- and postoperative recovery periods, bearing in mind the possible deleterious effects of corticosteroids on fresh intestinal anastomoses.

Steroid therapy might impair prognosis in surgery by increasing the hazard of infection. If infection is suspected, appropriate antibiotic therapy must be administered, usually in larger than ordinary doses.

General precautions common to all corticosteroid therapy should be observed during treatment with CORTENEMA, including those pertaining to growth suppression in children during prolonged use. Patients should be kept under close observation. If severe reactions or idiosyncrasies occur, steroids should be discontinued immediately and appropriate measures instituted.

If it is necessary to use CORTENEMA in pregnant patients, their infants should be closely observed for signs of hypoadrenalism; and appropriate measures, including administration of corticosteroids, should be instituted if such signs are seen.

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Adverse Reactions: CORTENEMA Hydrocortisone Retention Enema may produce all of the side effects known to occur with other forms of hydrocortisone therapy. These include moon face, buffalo hump, fluid retention, excessive appetite and weight gain, abnormal fat deposits, mental symptoms, hypertrichosis, acne, striae, ecchymosis, increased sweating, pigmentation, dry scaly skin, thinning scalp hair, thrombophlebitis, decreased resistance to infection, negative nitrogen balance with delayed bone and wound healing, menstrual disorders, neuropathy, peptic ulcer, decreased glucose tolerance, hypopotassemia, adrenal insufficiency, necrotizing angiitis, hypertension, pancreatitis and increased intraocular pressure.

In children, suppression of growth may occur. Increased intracranial pressure may occur and possibly account for headache, insomnia and fatigue. Subcapsular cataracts may result from prolonged usage. Long-term use of all corticosteroids results in catabolic effects characterized by negative protein and calcium balance. Osteoporosis, spontaneous fractures and aseptic necrosis of the hip and humerus may occur as part of this catabolic phenomenon.

Where hypopotassemia and the other symptoms associated with fluid and electrolyte imbalance call for potassium supplementation and salt-poor or salt-free diets, these may be instituted and are compatible with the diet requirements for ulcerative colitis.

Dosage and Administration: The use of CORTENEMA Hydrocortisone Retention Enema as an adjunct in the treatment of ulcerative colitis is predicated upon the concomitant use of modern supportive measures, such as blood replacement, rational dietary control, antispasmodics and sedatives, antibacterial therapy, and systemic steroids.

The usual dose is one CORTENEMA Hydrocortisone Retention Enema daily for two or three weeks and every second day thereafter, administered intrarectally in the evening before retiring. Every effort should be made to retain the medication for at least one hour, preferably all night. This may be facilitated by prior sedation and or antidiarrheal medication. If clinical or proctologic improvement fail to occur within two or three weeks, discontinue the drug.

For administration by retention enema, instruct the patient to lie on his left side during instillation. Shake the bottle vigorously to resuspend the insoluble portion of hydrocortisone. Expose the lubricated tip by removal of the protective sheath, grasping the bottle at the neck where it is most rigid. Carefully insert the lubricated tip into the rectum in the direction of the sacrum. Slowly express the contents by compressing the container. After instillation, the patient should remain on his left side for at least 30 minutes, to allow distribution of the medication throughout the descending colon and rectum.

For coverage of more distant segments of the colon, CORTENEMA Hydrocortisone Retention Enema may be diluted to from 100 cc. to 300 cc. with isotonic saline and administered by intrarectal drip.

The duration of treatment is dependent on the degree of response. If a satisfactory response is to be obtained, it usually occurs within five to seven days, as evidenced by a marked reduction of clinical symptoms. Improvement in the appearance of the mucosa, gauged by barium enemas and sigmoidoscopic examinations, may lag somewhat behind clinical improvement. The usual duration of therapy is two weeks, although some cases require therapy for longer periods (up to two or three months). Minimal control of symptoms is an insufficient basis for the prolonged use of CORTENEMA. If there is no clinical or proctologic response within two or three weeks, or if the patient's condition worsens, discontinue the drug.

Because of hydrocortisone absorption, proper precautions against unwanted systemic reactions or side effects should be observed. Symptomatic improvement, evidenced by decreased diarrhea, weight gain, improved appetite, lessened fever, and decrease in leukocytosis, may be misleading and should not be used as the sole criterion in judging efficacy. Actual sigmoidoscopic examination and X-ray visualization are most reliable. Since steroids can inhibit wound healing, enema or drip therapy should not be employed in the immediate or early postoperative period following ileorectostomy.

How Supplied: CORTENEMA Hydrocortisone Retention Enema is supplied in boxes of seven single-dose units.

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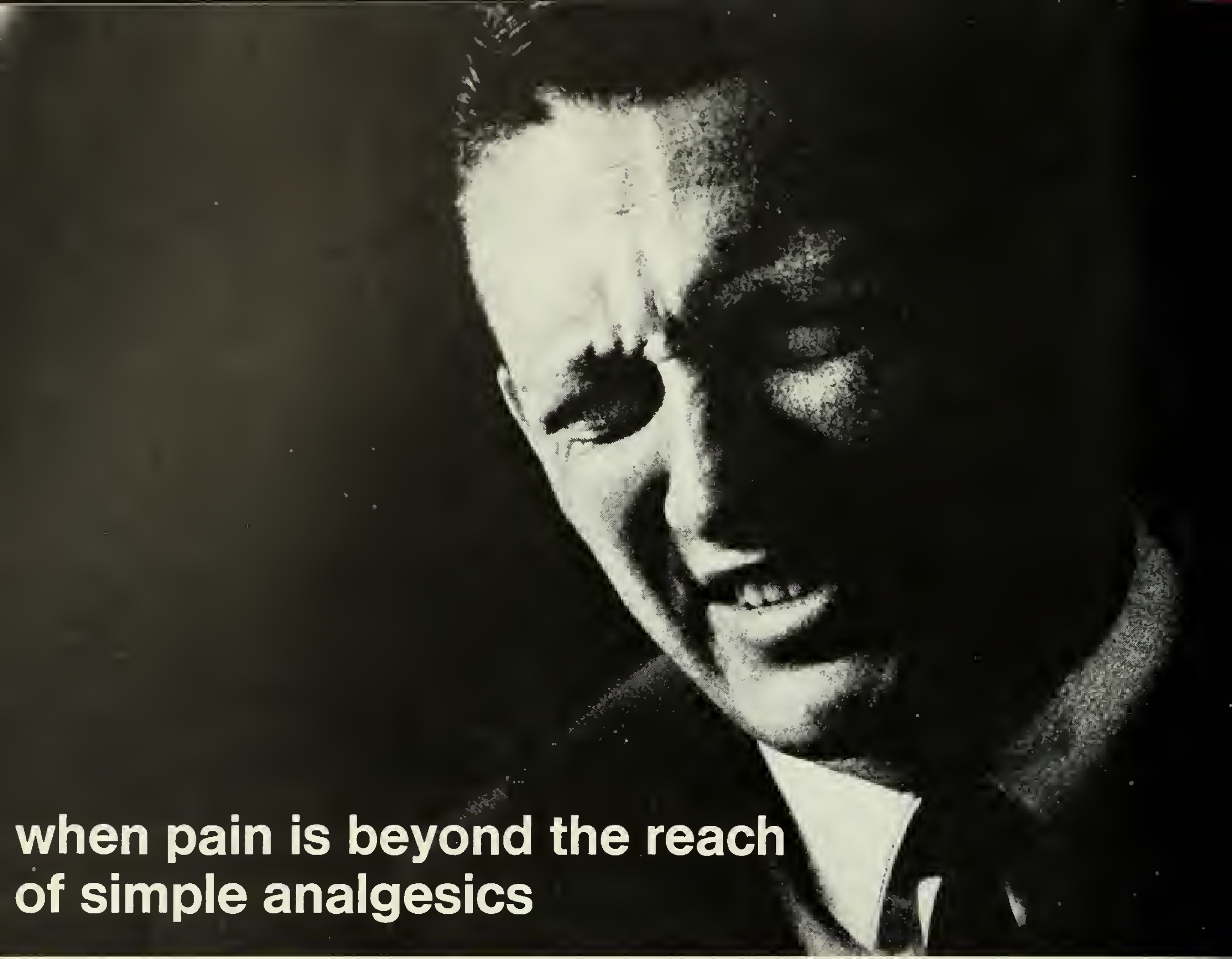
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1. Collective studies, Department of Medical Research, Winthrop Laboratories.

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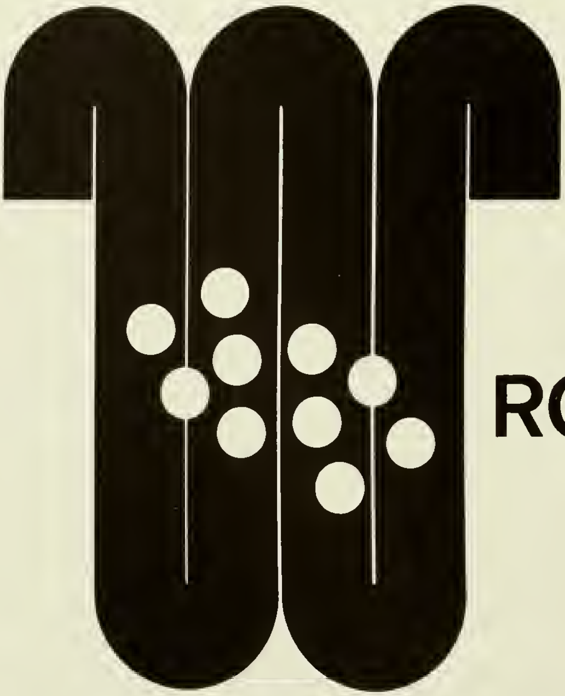

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*Neyroud, M.: Praxis 44:648-650 (July 14) 1955.

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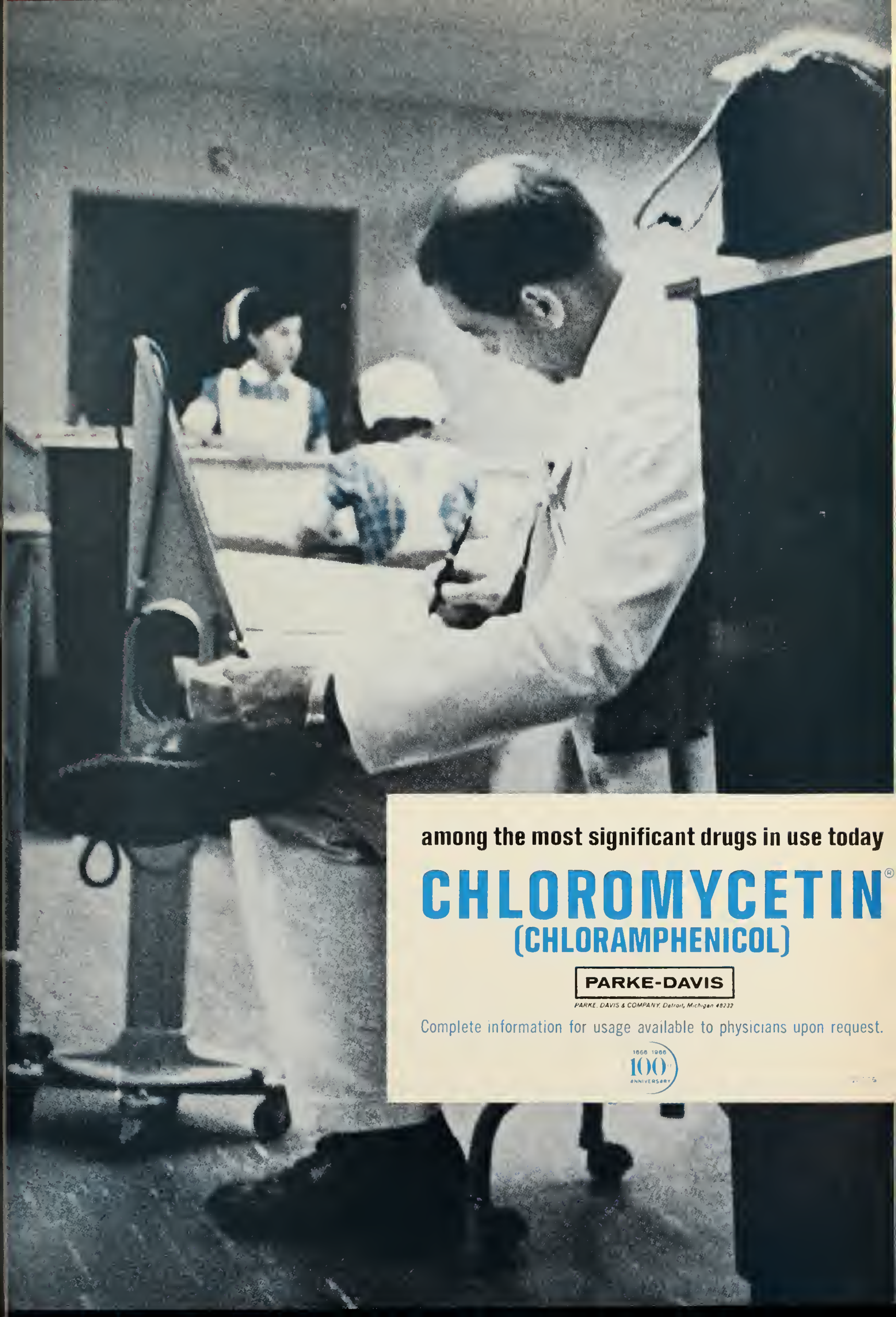

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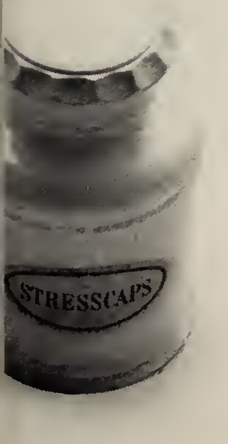

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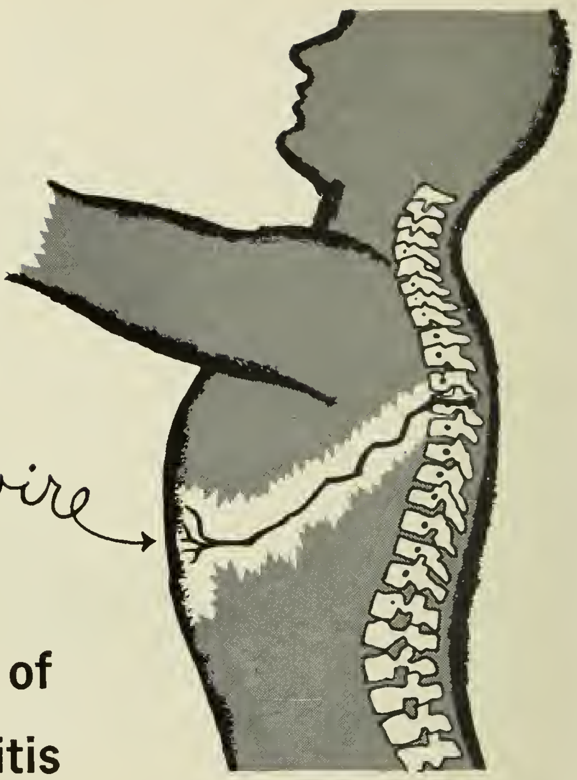

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this issue: emergency anesthesia and the common cold

When emergency anesthesia is complicated by the common cold

Barry Belonsky, M.D., F.A.C.A.
Staff Anesthesiologist, Hospital of The Albert Einstein College of Medicine, New York City

Medical facilities are often presented with unfamiliar patients who have unknown health histories. This is particularly true in emergency situations that arise due to accidents or acute illnesses. These cases may need prompt care requiring anesthesia, and if they involve colds, nasal allergies or other upper respiratory infections, can account for many complications which make up a major hazard during emergency anesthesia.

Administration of general anesthesia to a patient with a cold or upper respiratory infection is a hazardous undertaking. It should be avoided if at all possible. Indeed, the presence of U.R.I. is good reason for postponement of elective surgery.[1] In emergency surgery, regional or local block should be considered, but if general anesthesia is mandatory, it should be approached with utmost caution.

Since the attitude of "emergency surgery — hurry" has been replaced by "emergency surgery — watch out",[2] a knowledge of the complications is a great help in preventing them. Here is a brief outline of the problems involved and their treatment. Prevention of the complications is discussed later.

Complications during the induction of anesthesia

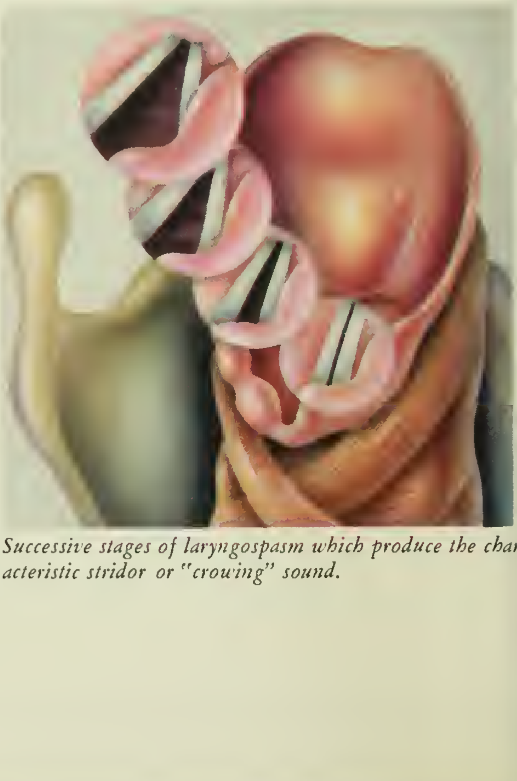
Most of the complications are a direct result of secretions and some a result of accompanying secondary infection. For example, *airway obstruction* due to excessive secretions occurs very commonly and is the direct effect of the cold. Respiratory exchange may be obstructed at any time during anesthesia because of excessive secretions, but is most likely to occur during induction. Suction apparatus must be available to overcome this.[3]

Excess secretions which stimulate and irritate the epiglottis and vocal chords can cause *laryngeal stridor and obstruction*. This can lead to complete laryngeal closure with resultant anoxia and death.

Bronchospasm and laryngospasm can result from secretions penetrating the bronchi and bronchioles. In laryngospasm, there are both inspiratory and expiratory stridor and difficulty in inflating the chest; in bronchospasm there is an expiratory wheeze, but not as much difficulty in inflation, although some resistance may be felt. Stridor is due to partial or complete closure of the vocal cords in spasm and the "crowing" sound is almost pathognomonic.

Secretions obstruct the nasal airways. This produces *difficulty in ventilation* through the mouth until the patient is deep enough to place an oral airway. An intravenous agent can be given to facilitate the induction of anesthesia.

Difficulties can arise if intubation is performed to ventilate the patient. For example, teeth can be broken by too vigorous attempts at intubation, or the intubation itself may be technically difficult due to secretions obstructing the view of the glottis. The postoperative sequelae of intubation ranges from mild laryngitis to pneumonia with atelectasis, and are seen far more commonly in patients suffering from colds than in normal patients.



Successive stages of laryngospasm which produce the characteristic stridor or "crowing" sound.

Progression of bronchioles into bronchospasm.

Complications during the maintenance of anesthesia

Bronchospasm can occur in an unintubated patient due to secretions entering the bronchial tree from above, and acting as an irritant to the bronchi and bronchioles. Secretions accumulate quickly and the patient has to be suctioned continually. The whole cycle of coughing, bucking, laryngospasm and bronchospasm may ensue. The difficult decision here is whether it is better to suction the patient continually or to use an endotracheal tube which protects the cords and bronchi but introduces the risk of attendant complications.

Postoperative complications

Postoperatively, complications can be more serious than even the intra-anesthesia complications, and occur much more frequently in a patient who has been intubated.[4]

Sore throat and pharyngitis can result both from the preoperative upper respiratory infection and from the drying of the mucous membranes which occurs during anesthesia.

Tracheitis and bronchitis often result from secretions trickling down the tracheobronchial tree.

Laryngitis is frequently seen in patients with upper respiratory infections who have been intubated. There is a significant increase in the incidence of laryngitis compared to that in patients without upper respiratory infections.

Subglottic edema is a condition which occurs mainly in children who have been intubated. This pathology results from an exudate developing in the areolar tissue just below the cords. Because of the small size of the child's trachea, even a 1 mm increase in size of the mucous membrane can severely impair the air passage. Children exhibit this by severe expiratory stridor and may even become cyanotic. This may so severely embarrass the child's breathing that it must be treated vigorously. Most authorities agree on the treatment[5,6,7,8] consisting of a high oxygen concentration in the inspired air (60%), plus high humidity (close to 100%). Adequate parenteral fluid intake and slight cooling of the body temperature (by a cooled oxygen tent) also help in mild cases. In severe cases, there may be hypoxia which increases the restlessness and the oxygen demand rises. Sedation is often necessary, although concomitant depression of the respiratory center is undesirable. An antihistaminic accomplishes this purpose well, and adds sedation. Since there is always a possibility that an allergic response plays a role in edema, some relief of the respiratory distress may occur. Steroids should be used to control inflammatory and allergic phenomena and swelling. If all this fails, and the patient is still restless and hypoxic, a tracheostomy should be performed immediately.

(concluded on following page)

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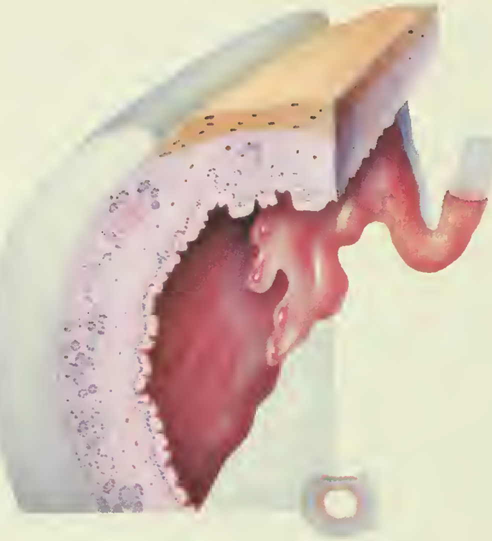

Cross section of trachea showing subglottic edema and lumen reduction due to mucous membrane congestion.

Pneumonia may also follow anesthesia administered to a patient with a cold. This can be caused by accumulated secretions becoming secondarily infected and causing consolidation of the lung. *Atelectasis* of the lung can result if one of the bronchioles becomes plugged by secretions, preventing aeration of the distal part of that lung. This is seen more frequently following upper respiratory infection because dry anesthetic gases aggravate the infection, causing secretions to change from watery to thick and viscid, and consequently difficult to suction.

Prevention of complications The first rule to prevent complications, of course, is to use a regional or local anesthesia whenever possible. But when emergency surgery is a must, in spite of the presence of a cold, allergy, or upper respiratory infection, here are some ways to prevent complications.

Give nose drops preoperatively. This can help shrink the congested nasal mucous membranes and reduce secretions for better air passage. (Results of this method are sometimes unsatisfactory because of the short duration of effect or rebound congestion.) For longer effect, oral antihistamines with nasal decongestants are often given to provide and maintain a drying effect on secretions.

To clear the tracheobronchial tree, instruct the patient to cough preoperatively. Cold steam or water nebulizers effectively humidify the nasal, pharyngeal and bronchial passages and often make the patient more comfortable. Tenacious secretions become more watery under humidification, clear more thoroughly preoperatively and are more easily suctioned from the airway during anesthesia.

Give intravenous fluids to those patients who appear dehydrated due to a cold. In a well hydrated patient the respiratory tract secretions are less viscid and more watery. This is particularly true in asthmatics.

Summary: Administration of emergency anesthesia to a patient with a cold or upper respiratory infection can lead to a chain of events that may result in increased postoperative morbidity and even death. This is because of the excess secretions formed in these conditions. Preoperative measures to prevent or reduce these secretions should be undertaken and will result in smoother and safer anesthesia.

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Auto-Amputation of the Hands and Feet

An Unusual Neurovascular Disease

WILL E. DONAHOE, M.D.
Sioux Falls, South Dakota

It is indeed most unusual to find in the medical literature a report of a patient who had such meticulous medical care from the day of birth, for a slowly but definitely progressive condition, until death at the age of 20 years and 6 months. The reader's attention is called to Dr. Donahoe's twenty years of extensive studies, scrupulous care, and arrangements for large numbers of medical consultations and periods of hospitalization in excellent medical centers. To have published a detailed record of all examinations, hospitalizations, and home care would have required several issues of this journal. Therefore, Dr. Donahoe has given us only the highlights. For lack of space, he has not included names of tests employed, and so forth, but obviously every conceivable test was done and every possible diagnosis was considered in the many comprehensive studies conducted in his office and in 3 eminent medical centers. This article also brings out the patient-doctor relationship, the problems of the patient and family, and the humane element.

J. A. MEYERS, M.D.
Chairman, Board of Editors

SHIRLEY JEAN WHITE became well known because of her severe, progressive, crippling condition with an ever-challenging diagnosis. Her pictures best show her condition, although they do not show her bright face nor reflect her happy disposition.

The case was first classified as a neurovascular condition of peripheral vessels, resulting in slow auto-amputation of all digits, metacarpals, metatarsals, parts of carpals, and tarsals, with eventual involvement of the nasal septum, ears, brain, and lungs. In addition to all local diagnostic attempts, she was studied at the Mayo Clinic in 1944, 1947, 1950, 1956, and 1962, as well as at the University of Minnesota for four months in 1950, eight months in 1951, three weeks in 1952, and six months in 1953. Locally, she was seen by visiting pediatricians, dermatologists, internists, orthopedists, and cardiovascular specialists from a dozen different medical schools and centers. Diagnosis could never be determined. In all these studies, every conceivable test and therapeutic effort resulted in failure. No known case or syndrome would fit Shirley, and no similar case had been reported in the literature.

Shirley was a normal, alert, white infant, born November 4, 1943, following an uncomplicated delivery. Her parents were moderately large, healthy, and active. As of this date, she has a brother, age 29, weighing 275 lb. and measuring 6 ft. 8 in.; a sister, age 25, weighing 180 lb.; and a younger sister, age 19, weighing 145 lb. All are of normal birth and healthy background. Her maternal grandfather, age 78, has had arthritis for twenty-five years. Her paternal grandfather is 74 and has had heart disease for twelve years. Her paternal grandmother died at age 54 of heart disease. Her father has had coronary heart disease for four years. Shirley weighed 9 lb. 4 oz. at birth, and she had a reddened tip of nose with a slight notch of the left ala, a small curled right ear lobe, and flushed cheeks. The ery-

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WILL E. DONAHOE *is clinical professor emeritus, pediatrics, University of South Dakota Medical School.*

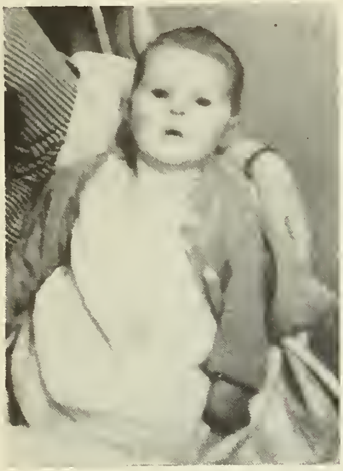

Fig. 1. Erythema of skin of cheeks and forehead at 6 weeks of age. Small notch of right ala nasi may be discernible.

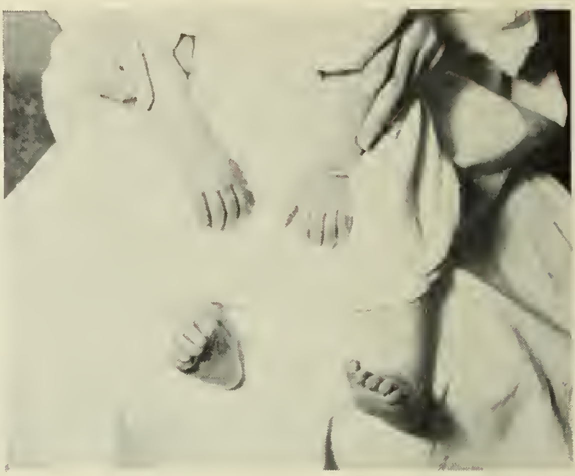

Fig. 2. Erythema of skin and swelling of toes and fingers at age 1 year

thema of the cheeks cleared after a week, only to recur periodically (Fig. 1). About the third day, a slight reddened area of a finger was considered an infected hangnail, and it cleared in a few days.

At 6½ months she was hospitalized with persistent flushing of cheeks and intense, well-delineated erythema of the lower two-thirds of the forearms. There was marked redness of the dorsum of the hands which faded after a week. However, the palms of the hands and feet remained intensely reddened, dry, swollen, painful, and tender. These areas spontaneously cleared somewhat. There never was any feeding problem but a poor weight gain. Acrodynia seemed the most likely diagnosis, but this was ruled out because Shirley's disease was too severe and lasted too long. Allergy also was considered but soon ruled out. She was returned to her home. During the next two years she was readmitted to the hospital four times with temperatures of 103 to 105° F., with more redness, severe pain, and tenderness of feet and hands, requiring very heavy sedation (Fig. 2).

I examined her at birth and saw her repeatedly in consultation until the age of 2, when she came under my care. Because of recurrence, she was hospitalized, where she remained until the age of 7 (Fig. 3). The temperature, pain, and tenderness subsided, but the intense redness of hands and feet persisted and required bandaging. Dry gangrene with repeated sloughing of a phalanx of a finger or toe resulted. This condition involved the skin, soft tissues, and bone. With every recurrence, the temperature would subside, but the deeply inflamed distal parts would have to be continually bandaged to protect the area and ease the pain and tenderness. Each recurrence was equally severe for three to five days and was followed by the usual sloughing of another small distal part. Similar episodes for no discernible reason would continue to recur spontaneously every one to three weeks. During those periods of this progressing affliction, inability to determine the etiology and diagnosis was always

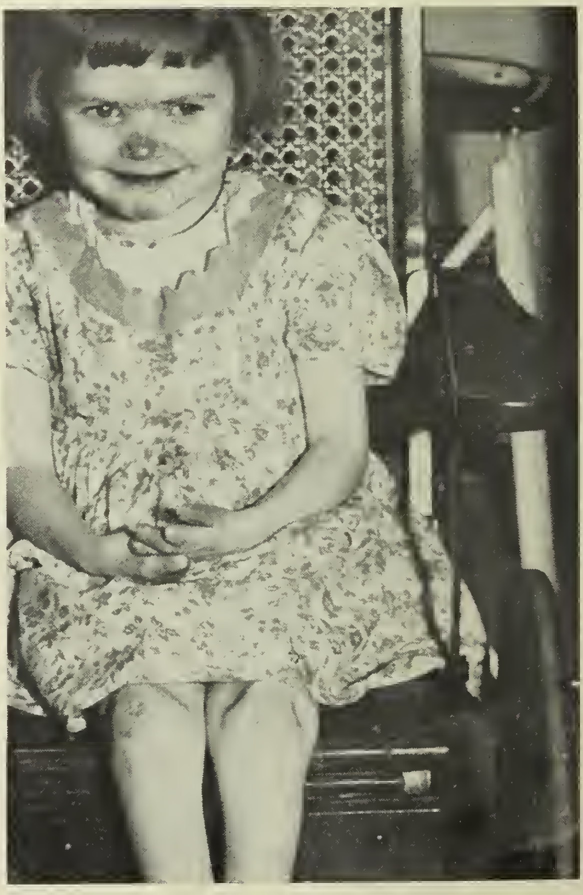

Fig. 3. Erythema of skin of nose, partial auto-amputation of digits of hands, and encrustation of knees at 6 years of age. It was feared that, because of early notching and periodic redness, the tip of the nose would be the first to go, but it was not.

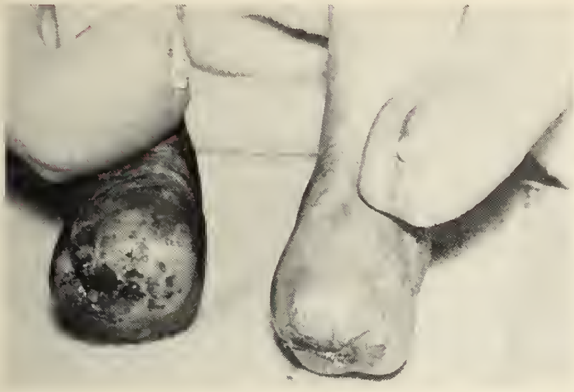

Fig. 4. Stubs of hands and feet at 12 years of age

the harassing problem. It was considered a self-limited condition, however, and was afforded symptomatic treatment. A few ill-advised prognoses were suggested.

At the age of 7 years, after being seen by a member of the University of Minnesota's pediatric staff, arrangements were made for her study there. Every conceivable test, with X-rays and repeated biopsies, proved nothing in the way of etiology or diagnosis. One significant finding was a hyperglobulinemia, but this led nowhere. Because of the wide interest in the case and the fact that nothing had been reported in the literature, there was a strong desire to report Shirley White as a case. However, certain journals were against case reporting. This then gave rise to the fear that some day this interesting case might be reported under an incorrect diagnosis. The study at the University of Minnesota led to several readmissions through 1952, and each readmission under a new resident meant a supreme challenge for complete study and diagnosis.

In 1951, a right dorsal sympathectomy was done with no beneficial effect. If anything, the right extremity was worsened. During this study, a very high AST led to the prophylactic use of penicillin each day. Up to this time, Shirley did have repeated attacks of pneumonia, and these were markedly lessened in occurrence and severity. During a study in 1952, she was given adrenocorticotrophic hormone (ACTH). As a result, her temperature was 105 to 107° F. for three weeks and she was comatose for ten days. Her life was despaired of and it was generally conceded that her mind was dulled a bit following this.

When Shirley began to sit again, she developed a comfortable position with her legs sharply flexed against her chest and her wrists hooked together like chopsticks around her ankles. The elbows and knees, as pressure points, became scaly and considerable encrustations followed. Controversies arose after several years, when the knees became ankylosed. Some doctors urged straightening and casts, but after more activity, such as in the wheelchair, only moderate ankylosis remained. Her skin was always very sensitive. Erythematous spots and areas recurred over the body, arms, and legs—sometimes slightly vesicular, but never pustular nor itching.

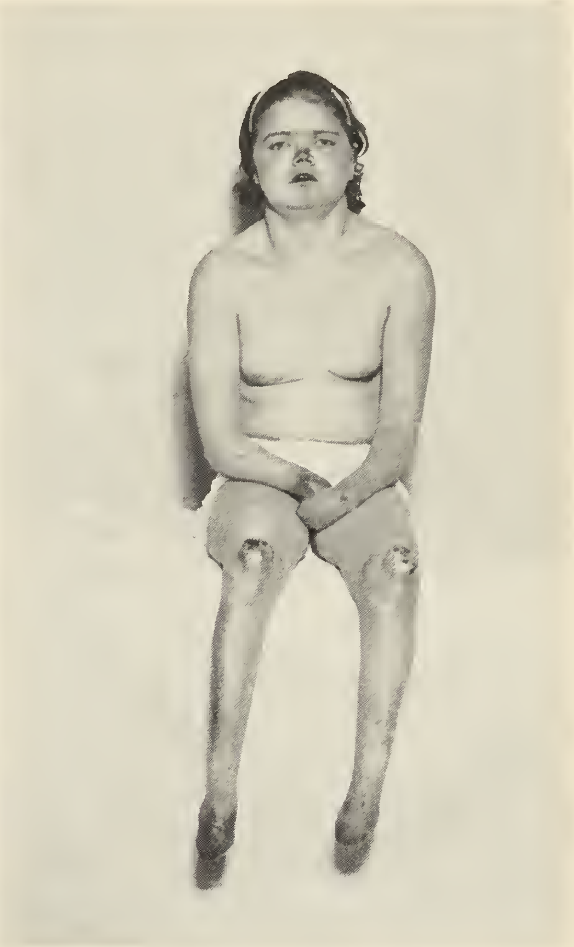

Fig. 5. Auto-amputation of digits and parts of the hands and feet. Discoloration of skin of legs, arms, and nose at 17 years of age

It was also remarkable that, while the recurring mild spells of pneumonitis probably were well controlled by the prophylactic penicillin, she did have considerable rhinitis and nasal congestion. At the age of 12 (Fig. 4), the nasal septum was found destroyed. She also had several periods of suppurative otitis media but no lymphadenitis. She did not contract colds or infectious diseases when others in the household were ill. Since hypogammaglobulinemia is a factor in susceptibility, the question might be that the hyperglobulinemia in her case was a factor in her resistance.

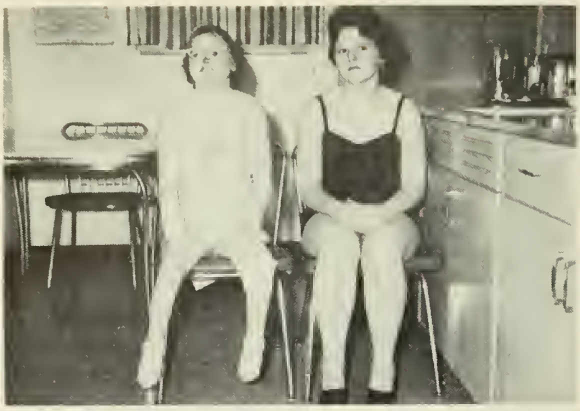

Fig. 6. Shirley at age 17, weighing 75 lb., with her 17-year-old, 125-lb. cousin. Heavy crusting of both knees. Knees and elbows subject to bruising when used to propel her across the floor; bandaging often necessary. Skin of legs shows some excoriation.

About the age of 13, her breasts filled out but there was no axillary or pubic hair. No menses followed and the breasts soon receded. Although she never made any appreciable weight gain, the patient remained small boned and fine featured and was never considered malnourished (Figs. 5 and 6). She would have periodic short spells of projectile vomiting unrelated to foods or meals. There was never any gastrointestinal distress, and her bowel and bladder habits were regular and normal.

Shirley White was a remarkable and fascinating girl. During her first seven years in the hospital, she attracted the attention of patients, nurses, and visitors. She became the direct charge of the supervising Sister, who disciplined her as any normal child and personally maintained Shirley's clothes closet. Her admirers gave her dresses and dainty clothing, and she loved to be kept clean and dressed in them. Because she had an alert mind, she was well aware of the condition of her ward mates. Through these and her later years, she was always respective of others, cooperative, and never spoiled by the attentions given her. She submitted to her painful episodes, never complaining nor showing temper at any time. Her belief in God and her acceptance of this condition were most thought-provoking to all who knew Shirley.

From the age of 7 until her death, she lived at home, where she received loving, devoted care. It was amazing what she could do for herself with her bandaged stubs of hands and feet. She could roll about the sofa or floor, handle a telephone, and be taken about in a wheelchair or car, which she enjoyed.

During these years, her hands and feet were regularly inspected and bandaged at the hospital. Every seven to ten weeks she was hospitalized with a temperature of 103 to 104° F., cough, and mild pneumonitis, which would subside in seven to ten days. Lung markings on X-rays showed increasing fibrosis.

In September 1961, the mother reported that Shirley had been having blackout spells for several months. Convinced of petit mal, an electroencephalogram showed a bizarre pattern of seizures which were thought to be due to vascular changes as found in the extremities and elsewhere. Before medication could be started, she was taken to Arizona to see if the climate would be beneficial. There she had one convulsion. After receiving phenobarbital and diphenylhydantoin sodium (Dilantin®), the convulsions stopped. The blackouts became less frequent in time and occurrence, however five months in a warm climate made no difference in the course of her disease.

In 1962, epidermolysis bullosa dystrophica was strongly urged as a diagnosis for Shirley. At the same time, this rare condition was widely discussed by dermatologists, and a case was published describing a 6-year-old girl with one extremity that resembled Shirley's. While some vesiculization had been associated with Shirley, bullae had never been observed.

On May 6, 1964, she was admitted to the hospital because of chills, fever, and scanty urination. She continued to be oliguric, and blood chemistries confirmed the diagnosis of acute uremia. No heroic treatment was instituted. The fever subsided and she felt better but then became anemic, developed hematemesis, and died peacefully four days later at the age of 20 years and 6 months. Urinalysis had always been normal on previous hospitalizations. For a few days during severe episodes, she would run a 4 + albumin with no cells or casts. In her last days, she showed no edema or mental confusion and, for the most part, she was her usual cheerful self.

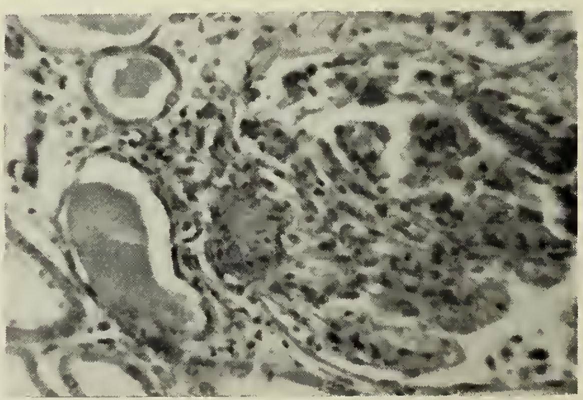

Fig. 7. Kidney, showing glomerulitis. × 430

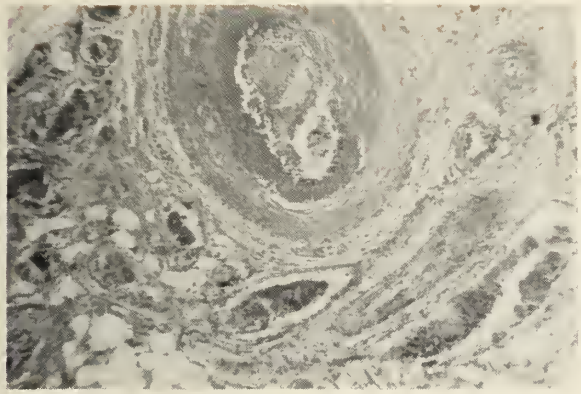

Fig. 8. Section of right stump. Medium-sized artery with fibrinoid necrosis and inflammation of the wall. × 100

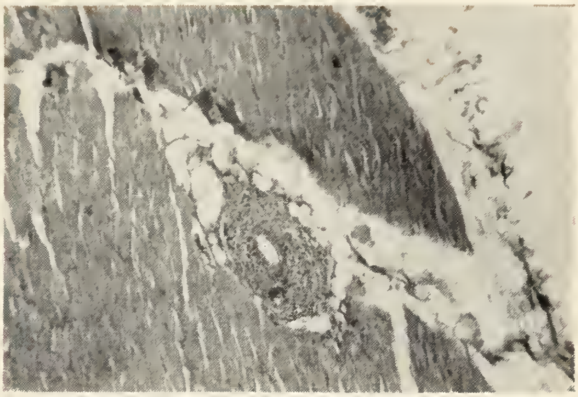

Fig. 9. Skeletal muscle. Small artery with mural and perivascular inflammation. × 100

She sat up and chatted gaily with attendants only a few hours before her death.

A complete autopsy was performed. We noted scarring and wrinkling of the ear lobe and posterior aspect of her right ear, as well as scarring and distortion of the tip of the nose and ala nasi. Her hands and feet were missing, and there was purplish-red discoloration of the skin; crusting of skin over the extremities, with areas of focal ulceration; and purplish-red discoloration of soft tissues of stumps of hands and feet, with softening and partial liquefaction of underlying bone. There was flexion deformity of the knees, with fixation. We noted bilateral fibrous pleuritis, with complete obliteration of both thoracic cavities; fibrous thickening of pleura with obliteration of interlobar fissures and diffuse nodularity of the lungs; and enlargement of kidneys, with diffuse petechial hemorrhages of the cortex. The kidneys weighed 210 and 190 gm.

Histologic examination revealed evidence of panarteritis involving arterioles as well as small and medium arteries within the lung, liver, gallbladder, stomach, intestine, kidneys, ovary, brain, periadrenal fat, and soft tissues of arm and leg stumps (Figs. 7, 8, and 9). Many vessels showed evidence of fibrinoid necrosis, with diffuse neutrophilic and mononuclear cell exudation involving all portions of the wall and perivascular tissues. A number of vessels within the right arm and leg stumps revealed vascular occlusion, with organizing and hyalinized thrombi. Pathology was essentially that of a disseminated polyarteritis nodosa with lesions in the acute, healing, and healed stages.

COMMENT

Autopsy findings have been reviewed by a dozen of the men who have studied and followed this case. The exhaustive extent of all studies must be realized. This report, for the sake of brevity, is a factual account of the clinical manifestations of this little girl. At any given time throughout her life she could have been reported as a case, meeting the highest standards required of detail, charts, tests, and other determinants. Although she was seen by many specialists, a final diagnosis was not made until the pathological findings were disclosed. The conclusion is polyarteritis nodosa, which was always considered as the most likely diagnosis but was ruled out first because of earlier biopsy findings and later because of the duration. While this disease is not wholly understood today, the question now is whether this was the basic cause of her condition or, rather, a terminal manifestation. In 1962, the diagnosis of epidermolysis bullosa dystrophica was advanced but there was no concurrence by the other consultants, including dermatologists who had first seen her.

It is a rare privilege for a physician to follow so interesting and puzzling a case from birth to death. I wish to emphasize that Shirley was the darling in every hospital and in her home. She was always most cooperative in all that was done for her and never showed temper, distrust, or unwillingness. She was always happy to be shown to the medical students and nurses and at medical meetings.

I think it well to mention the same cooperation from her parents, who were most understanding and loyal. They were put under extreme pressures and repeatedly admonished by their families, friends, strangers, cults, and even physicians, regarding the professional care given Shirley. Some went so far as having her denied special schooling in spite of her good mind and strong desire to learn. The economic and financial cost might be noted, as well. Shirley's father was a postal employee, and his insurance took care of only a small part of the hospital expense, although the hospital administration was always considerate. At the Mayo Clinic and the University of Minnesota Hospital, her care was under special funds or grants. As her physician, I made no charge. The many visiting specialists and consultants were always pleased to see her. She could have had her medical care paid for by the state and welfare agencies, but her parents refused. To do so, they would have had to accept the state's appointed physician. The parents' loyalty and Shirley's trusting friendship were such that it proved to be a most self-satisfying experience.

The author wishes to thank Dr. Paul Dwan, who initiated her care at the University of Minnesota, and Dr. Edmund C. Burke of the Mayo Clinic. Also, he is grateful to the many consultants: the late Dr. Henry Helmholz, Drs. Roger Kennedy and H. M. Keith, the pediatric staff of the Mayo Clinic, and their consulting specialists; the University of Minnesota pediatric staff: the late Dr. Irvine McQuaire and Drs. Charles May (now of Bellevue), John Anderson, Robert Good, John Adams (at UCLA), Forrest Adams (at UCLA), and their consulting specialists; residents of the University of Minnesota Hospital: Drs. J. C. O'Brien, J. J. Galligan, E. F. Walsh, and W. L. Pew; and also to Dr. George Birch, New Orleans; Dr. Joseph Bilderback. Portland, Oreg.; Dr. E. A. Hines, Oteen, N.C.; Drs. J. B. Gregg, Edmund McGreevy, A. K. Myrabo, and T. R. Anderson, all of Sioux Falls; and the many visiting specialists of every field for their opinions and continued interests in Shirley White. In recent years I have attended no national medical meeting without being sought out for information on Shirley.

Book Reviews . . .

Neuro-ophthalmology: Symposium of the University of Miami and the Bascom Palmer Eye Institute

compiled and edited by J. LAWTON SMITH, M.D., *278 pp., ill., C. V. Mosby Co., St. Louis, 1965. $21.75*

The material in this book was presented at the second postgraduate symposium on clinical neuro-ophthalmology sponsored by the department of ophthalmology, University of Miami School of Medicine, January 1965. The participants in this symposium were asked to speak on the subject of most active current interest to them. The volume thus presents unrelated but current topics in neuro-ophthalmology. The men presenting these various topics are experts in their fields of interest and the presentations are of uniformly high caliber.

Dr. J. Lawton Smith in his chapter on seronegative ocular syphilis and neurosyphilis stresses that clinical syphilis may be seronegative and points up the usefulness for specific treponemal tests. He feels that the indications for specific treponemal tests in ophthalmologic practice include any abnormal pupil, traumatic dislocation of the lens, uveitis, retinitis pigmentosa-like fundi, and optic atrophy. There is an additional chapter by Dr. Smith and his co-workers on experimental seronegative syphilis.

Dr. David G. Cogan gives an excellent summary both clinically and pathologically of the heredodegenerations of the retina. The use of serial photography of fluorescein in the circulating blood of the human ocular fundus makes exciting reading. The pictorial evidence of the various fluorescein patterns is convincing and it appears that fundus photography with fluorescein will add greatly to clinical differential diagnostic possibilities. For example, malignant melanomas of the choroid seem to show a fluorescence in the arterial phase and staining in the late venous phase while nevi show no fluorescence at any phase of the study unless there are overlying drusen. For those who are interested, there is a short chapter on the details of the technique necessary to produce these pictures. Dr. Frank B. Walsh has an interesting chapter on selected visual field studies. His comments on certain visual fields and their clinical correlation are most worthwhile. Dr. Robert W. Hollenhorst, who has made such a large contribution to the neuro-ophthalmologic understanding of strokes, has a good chapter on this subject. The importance of this subject is emphasized in the following quotation from Dr. Hollenhorst's comments: "About 40% of strokes result from atheromatous occlusion of extracranial branches of the aorta. The other 60% include embolic phenomena, hypertensive intracerebral hemorrhage, and ruptures of aneurysms of congenital malformations. This presentation will be confined to the problems associated with occlusive phenomena. Eighty to ninety percent of these patients have ocular manifestations." Additional good chapters on vascular topics are those of Dr. Thomas R. Hedges on modern concepts of occlusive vascular disease in ophthalmology and Dr. Noble J. David's chapter on neuro-ophthalmology of the occlusive disease in the vertebral basilar arterial system.

Dr. Richard Lindenberg has a comprehensive chapter on the neuropathology involving the lateral geniculate bodies, the optic radiation, and calcarine cortex.

A great deal of information, anatomic, physiologic, and clinical is present in the chapter entitled "The Neurology of the Orbicularis Oculi" by Dr. William Fletcher Hoyt and Dr. John Dennis Loeffler. The final chapter is on the phakomatoses by Dr. J. Donald M. Gass. This chapter stresses the 4 classic syndromes which comprise this group and makes mention of certain other syndromes which show certain features in common with the phakomatoses.

In summary, this volume prepared by experts and directed at the clinician, is good reading for anyone interested in the general topic of neuro-ophthalmology. The physical book itself is attractive, inclusive of index, and has good illustrations. It is highly recommended.

IRVING SHAPIRO, M.D.
Minneapolis

(Continued on page 397)

Some Unusual Sources of Upper Gastrointestinal Hemorrhage

WILLIAM S. MIDDLETON, M.D.

Madison

Hemorrhage from the upper gastrointestinal tract constitutes one of the serious medical emergencies. From one of a series of causes it may range from minor to exsanguinating proportions. As a rule the origin may be readily established. On the other hand, the establishment of the point of bleeding may elude existing methods of diagnostic precision. Hemorrhages from esophageal varices and peptic ulcer are usually localized by their respective histories, physical findings, and X-ray and endoscopic examinations. One of the common causes of upper gastrointestinal hemorrhage, acute gastritis, is frequently overlooked in the quest for some less obvious explanation. To the curious minded, several obscure sources of upper gastrointestinal bleeding will have an unusual interest and must always be considered in this situation.

Illustrative of one aspect of this problem was the 38-year-old woman admitted because of recurrent hematemesis. An earlier episode had led to an exploratory laparotomy that failed to disclose the source of bleeding. Two illuminating details of the history afforded the answer. The patient had had repeated severe epistaxis since the age of 14 and there had been similar experiences in several generations of the family. The telltale telangiectasia of the mucous membranes of the lips, mouth, and nares concluded the diagnosis of familial hemorrhagic telangiectasia, that is the Sutton-Rendu-Osler-Weber syndrome. Interestingly, at the Veterans Administration Hospital, Poplar Bluff, Mo., two patients with this condition were presented at a single clinic. One of the two had also submitted to abdominal surgery in the fruitless search for the source of the hemorrhage.

Genetically familial hemorrhagic telangiectasia represents a simple dominant trait with defective vascular walls. This weakness leads to capillary and arteriolar dilatation. At times there are arteriovenous aneurysms. In addition to hemangiomata of the skin and mucous membranes, venous pools may exist in the lungs, liver, and spleen. The hemorrhagic tendency advances with years, but there is no distinction between the sexes. A moderate anemia is the rule. Rarely attendant pulmonary arteriovenous shunts may lead to polycythemia. In general the medical management is symptomatic, but an interesting suggestion has been made for the control of epistaxis. Ethinyl estradiol, 0.25 to 1 mg. per day, will stop this troublesome symptom by changing the character of the nasal epithelium.[1] It is not helpful in any other source of bleeding from this condition.

A remarkable coincidence of mucocutaneous pigmentation and gastrointestinal polyposis bears the eponymic designation of the Peutz-Jeghers syndrome. From the genetic standpoint it is a nonsex-linked dominant disorder. A single gene is responsible both for the pigmentary and for the polypoid changes. The sexes are equally affected. The pigment is melanin deposited in vertical bands in the epidermis. The polyps, which are true adenomata, are found predominantly in the ileum and less frequently in the colon. Rarely they appear in the stomach and pharynx.

The brown to black patches of pigment in the lips, buccal mucous membranes, and palate are most conspicuous. Recurring attacks of colic with succeeding diarrhea and constipation result from intussusception, either of the ileum or colon, induced by the engagement of the polyp in the peristaltic sweep. Occasionally hemorrhage from the stomach or intestine may complicate the polyposis. The temptation to emergent surgery should be rejected in a majority of instances, since intussusception on this basis usually corrects itself and the extent of the polyposis denies

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WILLIAM S. MIDDLETON *is with the Veterans Administration Hospital, Madison, Wisconsin.*

radical excision of the total area of involvement. Only in the presence of persistent obstruction or continuing hemorrhage should surgery be invoked.

An interesting source of upper gastrointestinal bleeding that may endanger life, attends violent retching after alcoholic or other excesses. With such strenuous muscular force the intraesophageal pressure may many times exceed the normal level of deglutition, but transmural pressure gradients rather than direct intramural force are operative in the resultant injury. Mallory and Weiss described tears through the mucous and submucosal layers of the esophagus to the muscularis. They may rarely extend into the mediastinal tissues. Recent studies exclude such an extension from the Mallory-Weiss syndrome. Occurring at or adjacent to the cardioesophageal juncture these rents usually measure 2 to 3 mm. by 20 to 30 mm.

The story of such incidents is characteristic. After a bout of heavy alcoholic or dietary intake there is vomiting of the material ingested—a significant detail. Then follows a sequence of violent retching commonly without unusual local discomfort. At times tearing pain is localized to the epigastrium and radiates to the lower thoracic spine. Hematemesis may be extreme, but it is always preceded by vomiting of the gastric contents. If included in this category, mediastinitis is a feared complication, fortunately less ominous since the advent of antimicrobial agents. Gastroscopy should be undertaken without delay, since X-ray studies may be unrevealing. Beyond the question of a doubt, the Mallory-Weiss syndrome of lesser degree is much more common than appreciated. A majority of such order will heal spontaneously without special attention to the local indications. In more serious circumstances, recognized and promptly closed by sutures, the prognosis is good. Broad spectrum antimicrobial agents should be used in all patients with this condition. Of 6 patients with Mallory-Weiss syndrome personally encountered, 4 recovered, 1 died of hemorrhage, and 1 died from mediastinitis.

The following clinical and pathological report represents in classical detail another entity that deserves especial consideration in the present connection.

CASE HISTORY*

A 39-year-old man had experienced diarrhea of 8 to 9 stools a day for three years. The stools were yellow, foamy, and foul. In this period he lost 30 to 35 lb. Ten months before admission he suffered a sudden knife-like pain in the upper abdomen that radiated to the back. Eighteen hours later he was operated upon. A perforated jejunal ulcer was disclosed and 5 cm. of the jejunum were resected. Histologic section showed only an inflammatory reaction. Thereafter, there was a further loss of 35 lb. A diagnosis of nontropical sprue was made and the gluten-free diet with folic acid supplement was apparently attended by slight improvement. Four months before admission the patient was troubled with a severe gnawing pain in the epigastrium that radiated to the back. This pain was worse between midnight and 2 A.M. Milk gave some relief. The position of greatest comfort was lying on the side with his back against the wall, knees and thighs flexed, and a pillow held tight to the abdomen. The conventional ulcer regimen of diet, antacids, and antispasmodics was unavailing. A week before admission, headache and dizziness first appeared. Hematemesis and melena were marked. Weakness progressed. The tongue became sore.

On physical examination the significant details included marked pallor, a smooth tongue, and slight epigastric tenderness.

The laboratory findings of note were hemoglobin, 5.1 gm. per 100 ml.; hematocrit, 21%; marrow, normal.

Stools—blood present.

X-ray—slight deformity of the duodenal bulb; pooling with local narrowing in jejunum.

Gastric contents—volume 400 to 500 ml.; free hydrochloric acid, 75°.

With the continuance of symptoms and a progressive decline, laparotomy was again performed. Twenty-four centimeters of the jejunum were resected. The postoperative course was marked by a hypokalemic alkalosis after a month. Then massive gastrointestinal bleeding occurred and 35 transfusions were given in a futile attempt to stem the tide.

At necropsy there were 20 to 25 chronic ulcers of the jejunum, one of which had perforated with a generalized peritonitis. An islet-cell adenoma of the pancreas and a metastasis to a mesenteric lymph node completed the significant findings.

The clinical encounter with this patient anticipated the significant report of Zollinger and Ellison.[2] These workers cited the singular concurrence of unusually placed obstinate ulcers of the upper gastrointestinal tract and nonbeta-cell adenoma of the pancreas. At first they erroneously assumed that glucagon was the responsible abnormal product. Subsequent studies have proved that these adenomata and their metastases—liver, spleen, gastric and duodenal wall, and lymph nodes—produce an element akin to, if not, gastrin. This substance stimulates the parietal cells with the resultant excessive secretion of hydrochloric acid without affecting the production of pepsin. By appropriate studies of the denervated pouch of the dog's stomach, these results have established the humoral nature of the stimulation.[3,4]

Transferred to the clinical problem of the patient with the Zollinger-Ellison syndrome, its existence should be suspected when extreme intractibility or recurrence of obstinate symptoms attends adequate measures for the control and treatment of peptic ulcer disease. Add to this the unusual location of the ulceration and the fat is in the fire. Certain laboratory returns supply substantial evidence to support the diagnosis,[5] for example:

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*Reproduced through the courtesy of Dr. Richard A. Marshall, Veterans Administration Hospital, Oklahoma City.

Basic gastric secretion
- volume > 170 ml. per hour
- free hydrochloric acid concentration > 100 mEq. per liter
- total acid output > 17 mEq. per hour

Ratio of basic secretion to maximum acid output (MAO) after augmented histamine test: Ordinary peptic ulcer—basic 35 to 45% MAO, Zollinger-Ellison syndrome—basic 60% + MAO.

For patients with Zollinger-Ellison syndrome resisting ordinary medical management, logical treatment is early surgery. Theoretically, removal of the pancreatic adenoma should afford relief, but, although a few successes have followed this approach, a great majority of patients so treated have had temporary, if any, improvement from this simple procedure. Clearly the failures may be anticipated from the cited humoral activity of metastases. Experience now favors a therapeutic approach to the target organ, the stomach. Total gastrectomy is now recommended as the most certain measure of control of this condition.[6]

SUMMARY

Four unusual sources of upper gastrointestinal hemorrhage have been cited. By a strange coincidence all are designated by the names of particular contributors to their recognition and understanding, that is, Sutton-Rendu-Osler-Weber, Peutz-Jeghers, Mallory-Weiss, and Zollinger-Ellison syndromes. Yet their appreciation is more than an eponymic exercise. Any one of them may lead to grave loss of blood. Singularly, while surgery is rarely indicated in patients with familial hemorrhagic telangiectasia and Peutz-Jeghers syndrome, it may be imperative and lifesaving in the Mallory-Weiss and Zollinger-Ellison syndromes. Diagnostic awareness of these conditions with their management is a challenge to every physician.

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BOOK REVIEWS

(Continued from page 394)

Progestagen Therapy

by MAXWELL ROLAND, M.D., *88 pp., ill., Charles C Thomas, Springfield, Ill. 1965. $9*

This monograph containing 14 dosage tables, 20 figures, and 9 color plates is a concise source of information on the progestagens. It was written for physicians who wish to use this group of medications for a variety of indications. Chapters are devoted to the chemistry, pharmacology, and physiologic considerations. The numerous compounds are listed with suggested dosage schedules.

In the chapter on fertility control the selection and management of patients is carefully covered. Necessary laboratory studies, which I venture to guess many physicians ignore, are listed and contraindications emphasized.

Progestagen therapy in the treatment of menstrual disorders such as dysfunctional bleeding, dysmenorrhea, and secondary menorrhea are outlined along with a chapter on medical management of endometriosis with specific recommendations.

The authors feel there is a place for progestagens in the management of infertility and habitual abortion although there is little solid evidence to support this belief.

The use of these chemicals in (1) diagnosis of pregnancy, (2) delaying menses for various reasons such as weddings and swimming events, (3) premenstrual tension, (4) Stein-Leventhal syndrome, and (5) menopause is suggested. The final chapter is devoted to future uses such as the effect of these drugs on adenomatous hyperplasia and possibly adenocarcinoma of the endometrium.

On page 26 the authors cite a case of a 64-year-old patient being treated for vaginal bleeding with norethynodrel-mestranol (Enovid®) empirically without previous curettage. On page 45 they state that undiagnosed bleeding from the genital tract is also a contraindication for the use of progestagens. As the *New Yorker* would say, "Keep your mind on the theme."

They also state, "Provided that patients are carefully selected for treatment, none of the known side effects of progestagen therapy is of serious consequence." Enovid® has been shown to have a diabetogenic effect in at least 1 well controlled study. This might give pause to some physicians when considering this preparation in family planning for patients with an unfavorable history of diabetes in the antecedents.

No mention is made of the change in the hydrogen ion concentration in the vaginae of women on progestagens. This is not a lasting effect but is responsible for the frequently troublesome monilial infections occurring in patients on these drugs.

While I do not share the author's enthusiasm for these medications, the monograph is well organized, easy to get through, and well worth reading.

G. WILSON HUNTER, M.D.
Fargo

(Continued on page 403)

Uninhibited Antidromic Vasodilatation in Bronchiogenic Pathophysiologic Diseases

GEORGE S. HACKETT, M.D.
Canton, Ohio

Contributions throughout a century by distinguished scientists provided a basis for the prolonged meticulous and brilliant investigations by the late Harold G. Wolff;[1] by Sir John Eccles,[2] recipient of a 1963 Nobel award; by Borje Uvnas;[3] and by their assistants and others in clarifying neurovascular, stimulus-response activities that provide a logical hypothesis of the basic heritable physiologic mechanism by which oxygen and other hemic substances are sufficiently supplied to cells in the local stimulated area by spinal and cranial afferent impulse potential which is redirected by presynaptic axon reflex for antidromic vasodilatation of nutrient arterioles in response to the intensity and duration of sensory stimulation, uninhibited by outside influence. It is applicable to the evaluation of abnormal clinical manifestations and activities that contribute to hyperplastic and inflammatory degenerative, proliferative, and mutative functional disease processes in various systems and tissues when the physiologic mechanism becomes unbalanced in response to prolonged overstimulation of afferent potential and vasodilatation-diffusion of hemic substances in excess of tissue tolerance.

NEUROVASCULAR MECHANISM

Wolff[1] revealed that while a portion of the afferent impulse potential is conducted through synapse to the spinal cord or cerebrothalamic areas, or both, for integration, another portion of the afferent potential from the same stimulation with which this article is specifically concerned does not reach synapse but is redirected peripherally by presynaptic axon reflex between the terminal endings[4] and fibrils and conducted in antidromic (opposite) direction in the same and neighbor fibers[5] as a positive feedback to the walls of nutrient arterioles in the area of stimulation. There, within the walls, the potential stimulates the release of neurohumoral and chemical substances which initiate a vasodilatating increase of permeability for the transudation-diffusion of plasma containing oxygen, neurohormones, enzymes, proteins, chemicals, and other hemic substances including possible contaminants to within the perivascular interstitial tissue for permeating the membrane of cells for their physiologic activities of excitation, function, metabolism, rehabilitation, and reproduction (Chart 1 and Fig. 1).

Concerning vasoconstriction and vasodilatation, Uvnas[3,6] revealed that vasomotor control operates mainly through an increase or decrease of sympathetic vasoconstrictor influence and that centrally controlled vasodilators operate peripherally on paricapillary pathways. Also, peripheral arterial vasodilatation is a local phenomenon operating through sympathetic presynaptic reflex and antidromic conduction within the primary neuron. Eccles[2] made the important revelation that within the primary neuron there is no inhibition to the basic afferent potential concerned with antidromic vasodilatation except by a diminution of the stimulation that initiates the afferent potential, while Douglas

CHART 1

NEUROVASCULAR ACTIVITIES OF STIMULUS-RESPONSE MECHANISM

In response to etiologic stimulation of cells (muscle, epithelial) and their sensory receptors, afferent impulse potential is transmitted uninhibited within the primary neuron in two ways: [1] *through synapse* for spinal and cerebrothalamic integration and cerebral perception of sensation and [2] by *presynaptic axon feedback* for antidromic vasodilatation-diffusion of nutrient arterioles in the walls of arteries, nerves, muscle, and other tissue in the local area to supply oxygen and other hemic substances to cells for excitation, function, metabolism, rehabilitation, and reproduction (Fig. 1).

GEORGE S. HACKETT *is emeritus surgeon and research associate, Mercy and Timken Mercy hospitals, Canton Ohio. His address is 3214 Croydon Road N.W., Canton, Ohio 44718.*

CHART 2

UNBALANCED NEUROVASCULAR MECHANISM

In pulmonary tissues, prolonged overstimulation of cells, sensory receptors, and afferent potential and its reflex feedback for vasodilatation-diffusion of hemic stimulants, such as neurokinin and nicotine in excess of tissue tolerance, cause edematous inflammatory tissue reactions and excessive cell activities. These result in muscle and elastic tissue degeneration and fibrous proliferation in the walls of bronchioles, alveoli, and arterioles, accompanied by limited dilatation and contraction, hypoxia, and impaired ciliary activity; neuropathy, hypoxia, and homeostatic disturbances; and bronchial mucus–epithelial cell hyperplasia, metaplasia, and mutation. These are manifested by excessive unexpelled mucus contaminated with noxious stimulants and carcinogens, hypoxia, hyperplasia, and accelerated mitosis with intracellular disorderly rearrangements of protein molecules and diminution of genetic control in succeeding generations, with emphasis on more extensive proliferation in some cells, such as occurs in carcinoma. Other excessive afferent potential passes dynamically through synapse, causing homeostatic disturbances, and is perceived cerebrally as pain.

and Ritchie[7] found the primary afferent system is sufficient to changes in visceral environment and noted the predominance of afferent fibers in sympathetic nerves and in the 100,000 fibers of the vagus and some other cranial nerves. Eccles further revealed that inhibitory inputs act only on the synaptic endings of the primary afferent neuron.[3] This indicates that although the afferent impulse potential may have various etiologic origins the adequate supply of oxygen and other hemic substances is maintained locally by presynaptic axon reflex and antidromic vasodilatation in response to the intensity and duration of the primary afferent potential uninhibited by any outside influence.

UNBALANCED NEUROVASCULAR MECHANISM

Wolff revealed that prolonged overstimulation of afferent impulse potential and antidromic vasodilatation-diffusion of excess hemic substances resulted in nutrient arterial, perivascular, interstitial, edematous, and inflammatory reactions and excessive cell activities[1] which continue and progress as long as overstimulation of afferent impulse is maintained.[2] Wolff isolated a significant vasodilatating polypeptide which he identified as neurokinin. It is released during vasodilatation into the arterial wall and perivascular tissue where it accumulates during excessive activity. It was found to be a powerful vasodilator that increases capillary permeability, induces sterile inflammation and pain, and lowers the threshold for stimulation which is regarded as excessive operation of the normal mechanism for functional vasodilatation. Wolff's neurokinin appears 8 to 35 times normal[1,8] (Chart 2).

The nutrient arteriole perivascular inflammation within the walls of arteries may result in degeneration of muscle and elastic tissue, proliferation of fibrous tissue, diminution of arterial dilatability, contractility, luminal narrowing, and tissue hypoxia. In nerves, the inflammatory reaction may result in neuritis with fibrous tissue proliferation, hypoxia, lowered stimulation threshold, impaired conduction, and increased susceptibility to tissue damage. Accelerated cell activities result in increased function according to cell specificity such as mucus epithelial secretion and muscle contraction which are intensified by the inflammatory environment and may be in excess of genetic influence and tissue tolerance. Accelerated mitosis increases the cell turnover time of mucus epithelium which has been observed by Bertalanffy[9] for various systems and areas such as two days for the pyloric end of the stomach, less than two weeks for the gastrointestinal tract, and twenty-seven days for the replacement of bronchial epithelium with the turnover time further reduced in an inflammatory environment.[10] During continued acceleration of mitosis, the intracellular synthesizing rearrangements of protein molecules have been observed to become disorderly and resemble those in precancerous lesions.[6]

Eccles[2] further observed that as the other portion of excessive basic afferent impulse potential passes through the primary neuron synapse it predominates over inhibitory inputs as it is transmitted dynamically for integration in spinal or cerebrothalamic areas.

Afferent fibril receptors of the primary neuron are specially adapted to receive specific forms of stimulation such as tactile, pain, thermal, tension, light, sound, and others and to transform it into the initiation of afferent impulse potential. Recent contributions by Holmes, Khabarova, Hirsch, Miller,[11] and their associates have identified vagal and spinal sympathetic afferent and efferent nerve fibril endings and receptors distributed in relation to the muscle fibers of cardiac and coronary artery walls and sinus areas. Miller[11] made the important observation that the abundant, afferent, complex, unencapsulated receptors located within the myocardial fibrous attachments in the endocardium are receptors of tension which are morphologically and functionally homologous to similar endings throughout the body. These receptors have been variously referred to as "stretch," tension, and "bororeceptors." In this and similar presentations, they are designated as tensireceptors which seems appropriate because they respond to tension on fibrous attachments whether by contracting muscle, by traction on ligament or fascial attachments, or by traction on muscle attachments within the walls of a hollow viscus during distension such as in the heart, artery, gastrointestinal and urinary systems, and bronchioles. The initiation of excessive primary afferent potential and antidromic vasodilatation in response to prolonged overstimulation of tensireceptors has been applied clinically in the logical explanation of unbalanced physiologic mechanism in cardiovascular and other diseases[23] and is similarly applicable to pathophysiologic bronchial diseases. Increased products of cell metabolism and destruction cause lymphatic edema, inflammation, sclerosis, and obstruction.

Ungar's *Excitation*[6] with 1,240 references presents a comprehensive discussion of the various factors comprising the neurovascular physiologic activities of the stimulus-response mechanism and unbalanced activities and manifestations in this presentation.

This article is a correlation of valid contributions from various fields and from experimental and clinical observations[12,13] with others, including Wolff's cooperation in evaluating observations covering a considerable period[14,15] which was the impelling motive for this continuing investigation concerned with understanding man's basic functional activities and their clinical application to malfunctioning pathophysiologic disease processes. It emphasizes the etiology of afferent potential, its transmission and transfer processes, normal and disordered functional activities, and the pathologic tissue reactions and biologic activity that are observed when excessive activating forces predominate in unbalancing this basic primitive neurovascular stimulus-response mechanism of man and vertebrates[16] on which has evolved the phylogenic progression of fibers associated with man's sophisticated cerebral development.[7] It is further substantiated by valid factors encountered and provides a working hypothesis for evaluating clinical and experimental observations, invalid conclusions, and previously accepted unproved theories. It should be applicable to directing disease prevention and reversal by determining specific etiologic factors such as nicotine, which is implicated in noxious overstimulation of nerve, muscle, and mucus epithelial tissue in various systems.

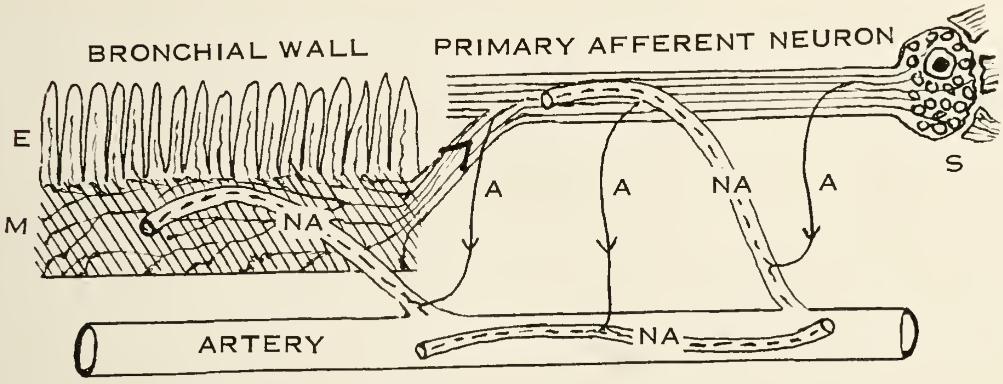
Functional disease processes of the bronchial tubes that result from activities within the province of the primary afferent neuron will be presented in detail. Other energizing, inhibiting, electrochemical, and cerebrothalamic energy transfer processes that contribute to homeostasis at or beyond the synapse of the primary neuron are not elaborated because their physiologic activities are outside the scope of this article, in addition to their becoming ineffective or modulated by the predominance of excessive afferent potential.[2]

BRONCHIAL NEUROVASCULAR MECHANISM

The bronchial neurovascular mechanism that supplies adequate oxygen and other hemic components to the cellular tissues for their activities is based on antidromic vasodilatation of nutrient arterioles in response to local stimulation and conduction of afferent potential in the primary neuron.[1] The afferent potential is initiated by specialized afferent receptors: in relation to mucus epithelial cells in response to exogenous stimulation by inhaled atmospheric components, in relation to endogenous stimulation by hemic components distributed to the cells by vasodilatation, and by tensireceptors (stretch) in contact with the fibrous attachments of muscle and elastic tissue in the walls of bronchial tubes and blood vessels which are activated by tension during expansion of the pleural cavity and by increased arterial blood volume. As previously described, the afferent potential is redirected by presynaptic axon reflex for antidromic vasodilatation-diffusion of oxygen and other hemic components including possible contaminants which permeate the membrane of cells for their excitation, function, metabolism, revitalization, and reproduction (Chart 1).

BRONCHIOGENIC PATHOPHYSIOLOGIC DISEASES

Accelerated bronchial activity with increased afferent impulse potential and antidromic vasodilatation of nutrient arterioles occur in response to overstimulation by strain and cardiopulmonary vascular disturbances, by endogenous excess of the hemic component neurokinin and contaminants such as nicotine, and by exogenous contact with epithelial cells by inhaled atmospheric contaminants such as esters, tars, dust, carcinogens, paper ash, and cigarette smoke condensate which are prone to accumulate in the dependent bronchial lumen[10,17] of man due to less effective ciliary action in expelling accumulated mucus which becomes a vehicle for noxious substances that perpetuate the stimulation of epithelial cells,[18,19] afferent potential, and antidromic vasodilatation and become a vicious circle (Chart 2).



PRESYNAPTIC UNINHIBITED ANTIDROMIC VASODILATATION

Fig. 1. E = epithelium. M = muscle, elastic tissue, nutrient arterioles, and nerve fibers. S = synapse and cell of primary neuron. Stimulated epithelial cells, muscle, and elastic tissue and their associated sensory receptors initiate afferent potential and its presynaptic reflex antidromic (A) feedback, for uninhibited vasodilatation of nutrient arterioles (NA) in local nerves, arteries, muscle, and epithelial tissue to supply adequate oxygen and other hemic substances for their activities. Other afferent potential passing through synapse (S) participates in spinal and cerebrothalamic activities of homeostasis and is perceived cerebrally as sensation.

It is postulated that bronchiogenic pathophysiologic diseases result from prolonged noxious stimulation of bronchial activity, afferent impulse potential, and nutrient arteriole antidromic vasodilatation-diffusion of excessive hemic substances as neurokinin[1,8] and possible contaminants such as nicotine into the perivascular interstitial tissue within the walls of arteries, arterioles, and nerves and within muscle, elastic, and epithelial cellular tissue. This causes interstitial edematous inflammatory reactions in excess of tissue tolerance[8] and results in impaired tissue metabolism and function, degenerative and proliferative processes, and excessive cell activities accompanied by a lowering of the threshold to stimulation and heightened susceptibility to damage, dystrophy, hyperplasia, and metaplasia. The manifestations in bronchial and arterial muscle and elastic tissue are degeneration with replacement by fibrous proliferation, which interferes with dilatation and contraction and results in hypoxia and neuritis with fibrous proliferation, lowered threshold to stimulation, and disturbance in conduction. Also, in epithelial tissue there is excessive function with hyperplasia, dysfunction of ciliary activity, accumulation of contaminated mucus, and accelerated mitosis with shortening of the turnover time of cells which may exceed the tolerance of genetic influence on the heritable synthesis of intracellular regulatory activities during transmission to successive generations and become a causative factor in the emergence of disorderly protein molecular sequence in genetic material in some cells by more extensive proliferation such as is observed in precancerous cellular changes. This is entirely compatible with the neurovascular stimulus-response mechanism of uninhibited antidromic vasodilatation which is consistent with Ewing's postulates and Horsfall's predicated biologic activity of genetic mutation in normal cells and explains the experiments by Rockey and associates[18,19] in making repeated applications of cigarette smoke condensate directly to the bronchial mucosa of 182 dogs with the aid of a bronchoscope including 29,000 applications in a five-year period that resulted in precancerous changes, carcinoma in situ, and one invasive carcinoma.

MANAGEMENT, PREVENTION, AND REVERSAL

Assuming that chronic bronchitis, emphysema, and bronchiogenic carcinoma may result from excessive uninhibited afferent potential and antidromic vasodilatation, their prevention and reversal should be directed to determining the individual etiologic factors applicable to prolonged noxious stimulation of pulmonary activity and eliminating them before irreparable pathologic changes are established.

DISCUSSION

Kimmel[20,21] observed the associated projection of afferent nerve fiber and artery within the progressively developing tissues of human fetuses. Others have recognized the continuing local collaborative activity of afferent fibrils and arterioles throughout life, such as in the repair of wounds. They substantiated Bishop's[16] conclusion that the basic heritable system of primary afferent fibers of vertebrates is rather complete at its functional level while others[4] observed the afferent potential conducted by presynaptic activity between interneurons and terminals for antidromic conduction and discharge of potential.

Man's basic neurovascular, physiologic, mechanistic response to local stimulation functions with facility within the limits of heritable tolerance while living judiciously. It is the continued overstimulation by inhalation, deglutition, and environmental activities that results in unbalanced pathophysiologic processes of various systems. The pathophysiologic processes of bronchial epithelial muscle and elastic tissue would appear to be applicable to similar prolonged noxious stimulation of the gastrointestinal and genitourinary tracts and to explain such lesions Guist[22] and associates designated as "ulcer vessel nests" in 77% of 48 chronic peptic ulcers resected from gastroduodenal walls which they described as a tangled network of thick-walled, tortuous, muscular, sclerotic, and partially occluded arteries and veins together with muscle bundles, lymphatic tissue, nerves, and scar tissue. This is an example of keen observation frequently reported, accompanied by "the mechanism is unknown." An understanding of the antidromic vasodilatating mechanism contributing to such disability would initiate interest in establishing the local etiologic factors and the adoption of appropriate management.

On the assumptions that excessive cigarette smoking over a period of twenty years may result in bronchiogenic carcinoma in susceptible individuals and that the twenty-seven-day turnover time of epithelial cells is reduced during prolonged overstimulation in an inflammatory environment there would be considerably more than 270 generations of cells in which the tolerance of genetic influence would be stressed and the intracellular molecular sequence in some cells would acquire rearrangements of mutation that contribute to more extensive proliferation in succeeding generations of daughter cells.

Although virus may contribute to carcinogenic disease through overstimulation, it has not been proved to comply with the criterion expressed by Horsfall and others as a biologic activity in being accepted by the cell as a gene that assumes control of the genetic apparatus responsible for its continued multiplication.

Man's physiologic adaptability to the duration of variations in atmospheric oxygen and pressure beyond the limits of his heritable environment to which he may be subjected in planned space flights has not yet been established. Any considerable variation in the amount and duration of oxygen content and atmospheric pressure on the respiratory and cardiovascular systemic systems would probably affect the stimulus-response mechanism of uninhibited afferent impulse potential and antidromic vasodilatation within some areas controlled by local afferent neurons and contribute to homeostatic unbalance.

SUMMARY

The basic heritable physiologic mechanism of man and other vertebrates consists of neurovascular stimulus-response activities in which afferent impulse potential is redirected in the terminal neuron by presynaptic axon reflex for uninhibited antidromic conduction to within the walls of nutrient arterioles for vasodilatation-diffusion of oxygen and other hemic substances to provide cell excitation, function, metabolism, rehabilitation, and reproduction.

Prolonged overstimulation of afferent potential and antidromic vasodilatation-diffusion of excess neurokinin and other hemic substances result in perivascular, interstitial, edematous, inflammatory degenerative and proliferative processes and accelerated cell activities in excess of heritable tolerance, accompanied by disturbances of function, hyperplasia, and metaplasia which provide a logical hypothesis of unbalanced neurovascular mechanism for pathophysiologic diseases of various systems.

Prolonged antidromic vasodilatation-diffusion of excessive hemic substances within the walls of bronchioles result in perivascular interstitial edematous inflammatory degeneration of muscle and elastic tissue and proliferation of fibrous tissue, neuritis, arteritis, excess epithelial cell function accompained by hyperplasia and accumulation of unexpelled contaminated mucus in the bronchioles, and accelerated mitosis with a shortening of the turnover time of cells and intracellular disorderly rearrangements of protein molecules such as are observed in precancerous lesions. They are the pathophysiologic manifestations of chronic bronchitis, emphysema, and carcinogenesis.

Reversal of the unbalanced neurovascular physiologic mechanism before pathologic processes have developed and the resumption of normal activities are attained by early identification and elimination of the etiologic factors responsible for prolonged noxious stimulation of afferent potential and antidromic vasodilatation.

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BOOK REVIEWS

(Continued from page 397)

Auscultation of the Heart

by BERNARD L. SEGAL, M.D., *and* WILLIAM LIKOFF, M.D., *198 pp., ill., Grune & Stratton, New York, 1965. $15*

Auscultation of the heart has come a long way since physicians first started to listen to the sounds generated by the heart and the blood moving within it. It is no longer sufficient to determine whether or not a murmur is present and, if it is, whether it is systolic or diastolic in time. With the great increases in our knowledge regarding murmurs, aided by refinements in phonocardiography and with the added information gleaned from cardiac catheterization, precise diagnoses undreamed of twenty-five years ago can now be made. The teaching of this art, and a precise art it is, is an essential part of the training of all students today.

Auscultation of the Heart by Drs. Segal and Likoff is a book intended to aid in teaching physicians and students alike the finer points in diagnosis one can make by listening to the heart carefully in an intelligent manner and with a sophisticated approach. It is obviously essential, as they point out, that the student bring maturity to his listening by repeated and repeated clinical examinations of more and more patients. Knowing what one will or should hear is no substitute for hearing it. On the other hand, listening and hearing without understanding what one is hearing or without knowing why these sounds are what they are, is learning by rote and is, therefore, meaningless and soon forgotten.

As the authors point out in their preface, examination of the peripheral circulation, the venous and arterial pulses and the precardium should be done before one listens, and these methods are described in the opening chapters. The remaining introductory pages are devoted to technique of auscultation, the stethoscope, and phonocardiography. Thereafter, the heart sounds are approached in a systematic manner according to their relationship to valve movements, the time sequences of the cardiac cycle, and to the abnormalities of these. The abnormal sounds generated or resulting from congenital defects are also discussed in detail.

The text is fairly brief and concisely written. Pressure graphs and phonocardiographic tracings, as well as heart sound diagrams, are liberally presented throughout the book. Anatomic drawings to illustrate both the locations of certain sounds on the chest, as well as the points of origin of the sounds in the heart, are numerous. Pertinent references appear at the end of each chapter.

Every physician who listens to a heart has an obligation to his patients to know the subject of auscultation. The student who is just learning clinical medicine will find this book invaluable once he has completed his basic clinical courses in anatomy, pathology, and physiology. The physician who learned the science of auscultation long ago will find this book a source of much new knowledge which will enable him to learn what it is he must look and listen for. The resident in medicine and cardiology will certainly find this a complete reference and an excellent source of information that he will use regularly.

Recordings of representative material to be used in conjunction with the text can be purchased from Grune & Stratton on both conventional records and tapes.

MILTON M. HURWITZ, M.D.
St. Paul

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Management of Juvenile Diabetes Mellitus

by HOWARD S. TRAISMAN, M.D., *and* ALVAH L. NEWCOMB, M.D., *147 pp., ill., C. V. Mosby Co., St. Louis, 1965. $12.75*

The cause, onset, management, and complications of diabetes mellitus vary considerably between children and most adults. The physician who chooses to accept the responsibility for the management of the juvenile diabetic must be interested in and informed about the condition. Drs. Traisman and Newcomb have provided the medical profession with a book that is both concise and informative. It is meant to serve as a reference for the clinical management of these children and intentionally does not delve into the basic concepts of the disease.

The book is well planned and contains a usable index. The number and quality of the illustrations and pictures are adequate to demonstrate the important points. The book contains a brief bibliography, but specific references to the medical literature are seldom made. The appendix contains cookbook instructions on the general nursing care of juvenile diabetics, the collections of specimens from these patients, and how to instruct parents. Fluid and electrolyte therapy is similarly outlined for the physician who uses the caloric and weight approach to intravenous fluid management. Physicians using other concepts are referred elsewhere.

This book should be of interest to medical students and busy physicians who wish to review the practical clinical aspects of the management of the juvenile diabetic.

DONNELL D. ETZWILER, M.D.
Minneapolis

Drugs and Nursing Implications

by LAURA E. GOVONI, R.N., FAYE CLARK BERZON, R.N., *and* MARILYN BELLINI FALL, R.N., *313 pp., Appleton-Century-Crofts, New York City, 1965. $4.95*

This is a quick reference paperback book on drugs written for the nurse practitioner and student to supplement a pharmacology text and highlight nursing implications. Alphabetically arranged according to generic name and indexed according to both generic and trade names, information on drugs commonly administered can be located easily and quickly. Emphasis is on physiological effect rather than on pathological indicatings for use. Some drugs are less thoroughly covered than others. In general, the drugs less thoroughly covered are those similar in action to drugs covered in detail. For example, sodium citrate is very briefly outlined since mention is made of its similarity to sodium bicarbonate; and only minimal information is given on omnopen (Pantopon®) with a reference to morphine sulfate which is covered fully.

Pertinent points on drugs are concisely outlined under the following headings:

1. Major category
2. Actions and uses
3. Absorption and fat
4. Contraindications
5. Toxicity and side effects
6. Dosage and route
7. Nursing implications

Reliable sources were used in the preparation of this text, and the authors have drawn upon their background of teaching in medical-surgical nursing for content covered under the heading "Nursing Implications." Points listed under this heading are not merely repetitions of those covered under other headings, but rather suggest those activities and responsibilities that the nurse assumes in the administration of drugs which, as stated by the author, relate to physical care, support of normal physiological processes, maintenance of normal body chemistries, preparation for treating overdose and toxic reactions, and patient and family teaching. When indicated, there is also a reminder that the continued administration of certain drugs is contingent upon laboratory findings and that preparation of the patient for specific clinical tests is an important nursing activity. A bibliography is included at the end of the book.

As stated in the foreword, the drugs presented are not all-inclusive. For example, some that are not mentioned are ethyl chloride, methyl salicylate, norethynodrel with mestranol (Enovid®), and pancreatic dornase. However, those included seem representative of the major categories of medicines in common use, exclusive of compounds and mixtures. The book does not include a glossary of terms used for categorization of drugs, nor a table of metric and apothecary equivalents. These seem to be omissions in a quick reference text on drug administration.

Because of the volume of drugs currently administered, this book should be useful to busy practitioners and students of nursing and medicine who wish a quick review of common drugs and their administration, and should serve as a reminder for pertinent points to stress with patients on self-medication.

VIRGINIA C. DERICKS

(Continued on page 17A)

ERRATUM. The support for the work reported in the article by M. D. Morris, Ph.D., D. A. Fisher, M.D., and R. Fiser, "Late-Onset Branched-Chain Ketoaciduria (Maple Syrup Urine Disease)," in the March 1966 issue of THE JOURNAL-LANCET (p. 149) was inadvertently omitted. The grant support was UC-ONR Contract No. 222-(51) to the University of California, The Clinical Investigation Center, U.S. Naval Hospital, Oakland, Calif.

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R. D. STORY	Fargo
PAUL BEITHON	Wahpeton
MACK TRAYNOR	Fargo
B. J. CLAYBURGH	Grand Forks
R. J. ULMER	Fargo
CLAYTON JENSEN	Valley City
R. D. McBANE	Devils Lake
W. T. POWERS	Grand Forks
J. J. MOSES	Bismarck
J. L. DEVINE	Minot
DEAN STRINDEN	Williston
J. W. JANSONIUS	Jamestown

Committee on Public Health

PERCY OWENS, Chairman	Bismarck
C. O. McPHAIL	Crosby
A. F. HAMMARGREN	Harvey
H. J. WILSON	New Town
R. F. GILLILAND	Dickinson
W. L. MACAULAY	Fargo
T. Q. BENSON	Grand Forks
L. H. KERMOTT	Minot
R. S. WOODWARD	Jamestown
G. U. IVERS	Fargo
D. H. LAWRENCE	Fargo
WM. BUCKINGHAM	Bismarck

Committee on Public Relations

WM. BUCKINGHAM, Chairman	Bismarck
F. A. DeCESARE, Vice-Chairman	Fargo
P. B. CURTIS	Jamestown
R. E. HANKINS	Mott
W. B. HUNTLEY	Minot
CLAYTON JENSEN	Valley City
DAVID JAEHNING	Wahpeton
RALPH MAHOWALD	Grand Forks
RALPH DUNNIGAN	Bismarck
L. E. BOYUM	Harvey
R. S. LARSON	Velva
WM. C. NELSON	Grand Forks
J. M. LITTLE	Mayville
W. R. FOX	Rugby
C. C. BORRUD	Williston
R. L. GESTON	West Fargo

Committee on Official Publication

J. W. CLEARY, Chairman	Bismarck
L. A. GILTNER	Minot
L. G. PRAY	Fargo

Committee on Medical Economics

O. V. LINDELOW, Chairman	Bismarck
J. F. HOUGHTON, Vice-Chairman	Fargo
V. J. FISCHER	Minot
E. J. BEITHON	Wahpeton
GALE RICHARDSON	Minot
KEITH FOSTER	Dickinson
R. E. MAHOWALD	Grand Forks
GEORGE HART	Minot
M. A. K. LOMMEN	Bismarck
R. H. LEIGH	Grand Forks
RICHARD RAASCH	Dickinson
JAMES MAHONEY	Devils Lake
JOHN GOFF	Fargo
E. J. LARSON	Jamestown
A. C. BURT	Fargo
P. L. JOHNSON	Bismarck
DEAN STRINDEN	Williston
S. E. SHEA	Minot

Committee on Scientific Program

Appointment Expiring 1966

DEAN STRINDEN	Williston
LLOYD RALSTON	Grand Forks

Appointment Expiring 1967

L. A. GILTNER	Minot
W. L. MACAULAY	Fargo

Appointment Expiring 1968

G. R. SWAFFORD	Jamestown
K. S. HELENBOLT	Grand Forks

SPECIAL COMMITTEES

Committee on Cancer

C. M. LUND, Chairman	Williston
J. N. ELSWORTH	Jamestown
O. W. JOHNSON	Rugby
GALE RICHARDSON	Minot
JOHN GILLAM	Fargo
WALLACE NELSON	Grand Forks
L. W. LARSON	Bismarck
ROBERT TUDOR	Bismarck
HARLAN LARSEN	Dickinson
ROGER BERG	Bismarck
G. L. COUNTRYMAN	Grafton

Committee on Nursing Education

G. W. TOOMEY, Chairman	Devils Lake
R. S. LARSON	Velva
NEILL GOLTZ	Fargo
C. A. BUSH	Beach
T. H. HARWOOD	Grand Forks
ALICE PETERSON	Bismarck

Committee on Maternal and Child Welfare

R. E. LUCY, Chairman	Jamestown
M. H. POINDEXTER	Fargo
JOHN GILLAM	Fargo
CARL BAUMGARTNER	Bismarck
BLAINE AMIDON	Fargo
R. T. GAMMELL	Kenmare
ALICE PETERSON	Bismarck
RALPH DUKART	Dickinson
J. W. JANSONIUS	Jamestown
THOMAS SCHAFER	Grand Forks
W. G. GARRETT	Bismarck
G. E. ELLIS	Williston

Committee on Foreign Trained Physicians

C. J. GLASPEL, Chairman	Grafton
JOSEPH SORKNESS	Jamestown
O. W. JOHNSON	Rugby
J. C. FAWCETT	Devils Lake
H. L. REICHERT	Dickinson

Committee on Diabetes

E. A. HAUNZ, Chairman	Grand Forks
DONALD BARNARD	Fargo
W. H. WALL	Wahpeton
B. HORDINSKY	Drake
WARREN JENSEN	Valley City
G. H. HEIDORN	Minot
E. O. HIEB	Jamestown
KEITH FOSTER	Dickinson
P. F. KLOSTERMAN	Bismarck

Committee on Crippled Children

PAUL JOHNSON, Chairman	Bismarck
C. W. HOGAN	Jamestown
A. E. CULMER, JR.	Grand Forks
D. T. LINDSAY	Fargo
B. A. MAZUR	Fargo
L. B. SILVERMAN	Grand Forks
G. M. HART	Minot
D. W. NAGLE	Fargo
J. M. LITTLE	Mayville
J. V. MILES	Jamestown
H. P. SMEENK	Bismarck
RALPH VINJE	Bismarck
J. V. EYLANDS	Rugby
GYMAN OKESON	Williston

Committee on Mental Health

A. C. KOHLMEYER, Chairman	Fargo
JOSEPH SORKNESS	Jamestown
G. H. HILTS	Cando
E. G. VINJE	Hazen
K. M. WAKEFIELD	Cooperstown
K. G. VANDERGON	Grand Forks
M. W. GARRISON	Minot
L. G. PRAY	Fargo
W. R. FOX	Rugby
M. A. K. LOMMEN	Bismarck
A. F. SAMUELSON	Bismarck
R. O. SAXVIK	Bismarck
LLOYD RALSTON	Grand Forks
HANS GULOIEN	Dickinson
E. J. LARSON	Jamestown
H. W. EVANS	Grand Forks
PAUL BEITHON	Wahpeton
M. J. OLSON	Williston
CLAYTON JENSEN	Valley City

Committee on Aging and Rehabilitation

HAROLD W. EVANS, Chairman	Grand Forks
BRIAN BRIGGS	Minot
T. E. PEDERSON	Jamestown
E. H. BOERTH	Bismarck
PAUL BEITHON	Wahpeton
PAUL AHLNESS	Bowman
E. P. WENZ	Fargo
DONALD LAMB	Fargo
BRUCE BEITHON	Fairmount
N. A. MACDONALD	Valley City

Liaison Committee to the North Dakota State Bar Association

PAUL JOHNSON, Representative	Bismarck

Committee on AMA-ERF

C. M. LUND, Chairman	Williston
K. G. VANDERGON	Grand Forks
JOSEPH CRAVEN	Williston
E. J. BEITHON	Wahpeton
R. D. NIERLING	Jamestown
T. H. HARWOOD	Grand Forks
F. D. NAEGELI	Minot
M. A. K. LOMMEN	Bismarck

Committee on Pharmacy

O. A. SEDLAK, Chairman	Fargo
E. L. GRINNELL	Grand Forks
NEIL MACDONALD	Valley City
E. G. VINJE	Hazen
O. V. LINDELOW	Bismarck
V. G. BORLAND	Fargo
P. H. WOUTAT	Grand Forks
W. C. HURLY	Minot

Liaison Committee to the Woman's Auxiliary to the North Dakota State Medical Association

RALPH MAHOWALD, Chairman	Grand Forks
G. A. DODDS	Fargo
J. D. CRAVEN	Williston
WM. BUCKINGHAM	Bismarck
G. W. TOOMEY	Devils Lake

Liaison Committee to the North Dakota Dental Association

DAVID JAEHNING, Representative	Wahpeton

Medical Center Advisory Council

P. H. WOUTAT, Member	Grand Forks

North Dakota State Advisory Council for Hospital and Related Construction

M. A. K. LOMMEN, Member	Bismarck

State Health Council

P. ROY GREGWARE, Member	Bismarck
R. F. GILLILAND, Member	Dickinson

Committee on Liability Insurance

JOSEPH SORKNESS, Chairman	Jamestown
P. H. WOUTAT	Grand Forks
O. W. JOHNSON	Rugby
O. A. SEDLAK	Fargo

Committee on Cardiovascular Diseases (Liaison Committee to the North Dakota Heart Association)

ROBERT STORY, Chairman	Fargo
R. M. FAWCETT	Devils Lake
KENNETH AMSTUTZ	Minot
MATT EHLEN	Fargo
P. ROY GREGWARE	Bismarck
CHARLES HAMILTON	Bismarck
JOHN BOYLE	Garrison
J. F. HOUGHTON	Fargo
A. M. CAMERON	Minot

Committee on Emergency Medical Service

RALPH MAHOWALD, Chairman	Grand Forks
DOUGLAS LINDSAY	Fargo
JAMES MURRAY	Fargo
PAUL AHLNESS	Bowman
W. C. HANEWALD	Dickinson
K. W. KIHLE	Bottineau
W. D. LaROCHELLE	Stanley
PERRY ENGSTROM	Wahpeton
J. W. GOVEN	Valley City
W. S. SKWAROK	Hehron
R. D. McBANE	Devils Lake
BLAINE AMIDON	Fargo

Crippled Childrens Services Division to the Public Welfare Board of North Dakota

D. E. SKJEI, Representative	Williston

Committee on Constitution and By-laws

KEITH FOSTER, Chairman	Dickinson
L. A. CHRISTOFERSON	Fargo
J. C. FAWCETT	Devils Lake
O. W. JOHNSON	Rugby
O. A. SEDLAK	Fargo

Committee on Medicine and Religion

M. J. E. JOHNSON, Chairman	Bismarck
FRANK MELTON	Fargo
G. H. HILTS	Cando
R. M. FAWCETT	Devils Lake
W. T. POWERS	Grand Forks
J. W. GOVEN	Valley City
P. ROY GREGWARE	Bismarck
T. E. PEDERSON	Jamestown
G. E. ELLIS	Williston
HARLAN LARSEN	Dickinson
R. K. HELM	Grand Forks
L. E. WOLD	Fargo
W. C. HURLY	Minot
NORVEL BRINK	Bismarck

Medical Advisory Committee to the State Highway Department

R. W. McLEAN, Chairman	Hillsboro
ROBERT IVERS	Fargo
W. C. HANEWALD	Dickinson
G. M. HART	Minot

Compact Board of Directors

P. O. DAHL, Chairman	Bismarck
G. CHRISTIANSON	Valley City
W. T. POWERS	Grand Forks
R. J. ULMER	Fargo
R. S. LARSON	Velva
W. C. HANEWALD	Dickinson
J. N. ELSWORTH	Jamestown

REFERENCE COMMITTEES

1. *To consider Reports of President, Secretary, Executive Secretary and Treasurer:*

ROBERT E. HANKINS, M.D., Chairman	Mott
ROY E. KULLAND, M.D., Vice-Chairman	West Fargo
C. ROBERT MILLER, M.D.	Bottineau
WILLIAM T. POWERS, M.D.	Grand Forks
RALPH DUNNIGAN, M.D.	Bismarck

2. *To consider Reports of Council, Councillors, Special Committees and the Report of the Representative to The Blue Shield Board of Directors:*

GEORGE L. COUNTRYMAN, M.D., Chairman	Grafton
R. DONALD McBANE, M.D., Vice-Chairman	Devils Lake
HENRY A. NORUM, M.D.	Fargo
BRIAN E. BRIGGS, M.D.	Minot
BLAINE F. AMIDON, M.D.	Fargo

3. *To consider Report of Delegate to the A.M.A., Medical Center Advisory Council and the Committee on Medical Education, and North Dakota Advisory Council for Hospital and Related Construction:*

JAMES V. MILES, M.D., Chairman	Jamestown
ROBERT J. ULMER, M.D., Vice-Chairman	Fargo
HAROLD W. EVANS, M.D.	Grand Forks
A. MALCOLM CAMERON, M.D.	Minot
CARL J. BAUMGARTNER, M.D.	Bismarck

4. *To consider Reports of Standing Committees, except Committee on Medical Education and Medical Economics:*

JAMES M. LITTLE, M.D., Chairman	Mayville
M. A. K. LOMMEN, M.D., Vice-Chairman	Bismarck
M. H. POINDEXTER, JR., M.D.	Fargo
RICHARD H. LEIGH, M.D.	Grand Forks
CLAYTON E. JENSEN, M.D.	Valley City

5. *To consider the Report of the Committee on Medical Economics:*

A. C. BURT, M.D., Chairman	Fargo
JAMES J. MOSES, M.D., Vice-Chairman	Bismarck
GEORGE H. HILTS, M.D.	Cando
KENNETH S. HELENBOLT, M.D.	Grand Forks
DONALD E. SKJEI, M.D.	Williston
RICHARD S. LARSON, M.D.	Velva

6. *Committee on Resolutions to include New Business:*

EDMUND G. VINJE, M.D., Chairman	Hazen
EDWIN O. HIEB, M.D., Vice-Chairman	Jamestown
LLOYD A. GILTNER, M.D.	Minot
JOHN A. SANDMEYER, M.D.	Grand Forks
PAUL J. BEITHON, M.D.	Wahpeton
WALTER C. HANEWALD, M.D.	Dickinson
PHILLIP O. DAHL, M.D.	Bismarck

7. *Committee on Credentials:*

RICHARD S. LARSON, M.D., Chairman (Also serves on Reference Committee No. 5)	Velva
CLAYTON E. JENSEN, M.D., Vice-Chairman (Also serves on Reference Committee No. 4)	Valley City

PROCEEDINGS: HOUSE OF DELEGATES SEVENTY-NINTH ANNUAL MEETING OF THE NORTH DAKOTA STATE MEDICAL ASSOCIATION

April 29, 1966 – Fargo, North Dakota

The first session of the House of Delegates of the North Dakota State Medical Association was called to order by the Speaker of the House, Dr. Lee Christoferson, at 9:00 A.M. in the Town House Motel at Fargo, N.D.

Dr. Richard S. Larson, Chairman of the Committee on Credentials, reported that all credentials were in order and that there was a quorum present.

Secretary Buckingham called the roll and the following delegates responded:

Doctors: H. A. Norum, Fargo; A. C. Burt, Fargo; Roy Kulland, West Fargo; Paul Beithon, Wahpeton; B. F. Amidon, Fargo; R. J. Ulmer, Fargo; N. F. Goltz, Alternate, Fargo; G. H. Hilts, Cando; R. D. McBane, Devils Lake; C. R. Miller, Bottineau; J. A. Sandmeyer, Grand Forks; G. L. Countryman, Grafton; K. S. Helenbolt, Grand Forks; H. W. Evans, Grand Forks; W. T. Powers, Grand Forks; L. A. Giltner, Minot; R. S. Larson, Velva; Brian Briggs, Minot; A. M. Cameron, Minot; C. E. Jensen, Valley City; J. J. Moses, Bismarck; M. A. K. Lommen, Bismarck; P. O. Dahl, Bismarck; C. J. Baumgartner, Bismarck; E. G. Vinje, Hazen; E. O. Hieb, Jamestown; J. V. Miles, Jamestown; D. E. Skjei, Williston; W. C. Hanewald, Dickinson; R. E. Hankins, Mott; J. M. Little, Mayville.

There were 30 delegates and 1 alternate delegate, duly authorized and present.

The following also attended the House of Delegates Meeting: Drs. C. H. Peters, J. D. Craven, R. W. McLean, J. R. Amos, J. M. Van der Linde, R. D. Nierling, T. H. Harwood, G. W. Toomey, V. J. Fischer, F. D. Naegeli, E. H. Boerth, R. C. Painter, Mr. Lyle Limond and Mr. J. Sherwood Williams, Representative of the Field Service Division of the American Medical Association.

The motion was made by Dr. Dahl, seconded by Dr. Ulmer, that the reading of the minutes of the previous meetings be dispensed with and that they be approved as printed in the Journal-Lancet. Motion passed.

Dr. Christoferson next referred all the reports printed in the Handbook to the proper reference committees for their action. He advised the members that all resolutions made by the Committees must be referred to the Resolutions Committee, No. 6.

REPORT OF THE PRESIDENT

So much remains to be done and so little time in which to do it. This was the reaction of your President when informed by the Secretary that this report was due by March 15 for publication in the handbook.

This has been undoubtedly the shortest year in my memory. It has been at one and the same time gratifying, frustrating, interesting and exciting and never dull.

It has been my great privilege to act as the Executive Officer of the State Medical Association the past year. I entered upon this assignment last May with a feeling of humility and with the resolve to fulfill the office one day at a time and thus avoid being overwhelmed by the problems that were bound to arise. I have found this approach to be a practical one and would recommend it to my successors.

I have responded to the best of my ability to all of the demands made upon me and my time by the office. These have included attendance at all regular and special sessions of the AMA, plus attendance at the State conclaves of our sister states of Minnesota and Montana, P.R. and AMPAC workshops at Chicago and Washington, D.C., and the North Central Medical Conference. I was privileged to attend the Conference of Presidents and other Medical Society Officers at the Pheasant Run near Chicago.

Our hospital dedication address was given by your President as well as addresses before the Auxiliary, most of the ten District Societies, one District Nurses Association meeting, the Governor's Committee on Employment of the Handicapped Convention, and all three service clubs in Williston. I was in attendance at numerour committee meetings of this Association. I mention these activities not with any sense of arousing the sympathy of my readers but rather to thank my colleagues in medicine in North Dakota for the privilege of serving in this office.

An added dividend for all of this activity is that one is soon on a first name basis with the porters and dining car stewards on the Empire Builder. The service station attendants between Williston and Bismarck have become my friends. Even airline personnel and stewardesses smile familiarly.

I cannot overstate the fine cooperation that has been mine from Lyle Limond who has been with me to smooth my path on most of the above mentioned forays. He has proven that a fine Executive Secretary can make an ordinary general practitioner acceptable in this responsible position. Thanks also to Lyle's staff for their helpful cooperation throughout this eventful year.

Respectfully submitted,
(Signed) JOSEPH D. CRAVEN, M.D., *President*
North Dakota State
Medical Association

SECRETARY'S REPORT

The following report of the Secretary is respectfully submitted:

MEMBERSHIP: The total membership for 1965 was 495. Of this number, 458 paid the regular membership fee, 1 paid 1/2 year's dues, 5 were on a limited basis, 7 were retired and 24 were Honorary. Five physicians passed away during the year and several have left the state. New members, however, are being steadily added to our roster.

Table 1 shows the annual membership for the past five years.

TABLE 1

COMPARISON OF ANNUAL MEMBERSHIP

	1961	1962	1963	1964	1965
Paid Memberships	436	436	449	455	459
Honorary Memberships	26	25	21	27	24
Limited and Retired	3	4	6	8	12
Dues Cancelled (age exemption, illness, military service)	1	1	1	1	–
	466	466	477	491	495

Table 2 shows the annual dues payments according to the cut-off date for preparation of this report for the past five years. The cut-off date of April 4, 1966 has given members a grace period of five weeks in which to pay their current dues, even though the Constitution and By-Laws of the Association states that all assessments must be forwarded to the Secretary not later than the 1st day of March of each year. You will note that even with the extension of time and despite the fact that members were urged to make dues payments as early as December, quite a large number of members are delinquent in dues payments.

TABLE 2

	May 1 1962	April 12 1963	April 3 1964	April 2 1965	April 4 1966
Paid-up Members	374	388	412	412	415
Honorary Members	25	21	25	22	26
To be Honorary	2	1	1	3	5
Dues Cancelled	1	–	1	–	–
Associate	–	–	–	1	2
Limited	–	2	3	2	2
Retired	–	2	2	5	8
	402	414	444	445	458

STATE ASSOCIATION MEMBERSHIPS

1965 Total Membership 495

Dist.	Reg.	Rtd.	Ltd.	Assoc.	Hon.
First	104	2	1	–	3
Second	38	–	–	–	2
Third	76	2	1	1	3
Fourth	58	–	–	–	5
Fifth	9	–	–	–	1
Sixth	91	1	1	–	5
Seventh	29	2	1	–	1
Eighth	21	–	–	–	–
Ninth	24	–	–	–	4
Tenth	9	–	–	–	–
	459	7	4	1	24

1966 Total Membership 453

Dist.	Reg.	Rtd.	Ltd.	Assoc.	Hon.
First	88	6	–	–	5
Second	36	–	–	–	2
Third	65	–	–	–	4
Fourth	49	–	–	–	4
Fifth	11	–	–	–	1
Sixth	80	1	–	2	5
Seventh	30	1	2	–	1
Eighth	21	–	–	–	–
Ninth	25	–	–	–	4
Tenth	10	–	–	–	–
	415	8	2	2	26

A.M.A. GENERAL MEMBERSHIPS

	April 4,	
	1965	1966
First	108	97
Second	38	37
Third	79	66
Fourth	60	51
Fifth	10	12
Sixth	97	87
Seventh	32	33
Eighth	19	21
Ninth	25	27
Tenth	9	10
	477	441

Representation in the House of Delegates is based on one delegate for each 15 paid-up members (or major fraction thereof), together with Honorary members. Delegates from the local societies should be seated on this basis so it is essential that dues be forwarded promptly.

The continued cooperation on the part of all members will be greatly appreciated.

Respectfully submitted,
(Signed) WM. M. BUCKINGHAM, M.D., *Secretary*
North Dakota State Medical Association

REPORT OF THE EXECUTIVE SECRETARY

GENERAL COMMENTS: Your Executive Secretary attended several State, Regional and National Meetings in behalf of the Association.

There are now three employees in the headquarters office since Mr. Daniel E. Buchanan left us on September 1, 1965 to seek a law degree at the University of North Dakota.

Mrs. Margaret Fremming and Mrs. Myrtle Kohler continue on as Office Secretary and Office Assistant respectively.

LEGISLATION: Since last reporting to you, the Medicare Bill passed both Houses of Congress and was signed by President Johnson. It is now known as Public Law 89-97.

Another Bill of great interest to the medical profession was also passed during the first session of the 89th Congress. It is cited as the "Heart Disease, Cancer, and Stroke Amendments of 1965." This piece of legislation was also called the DeBakey Bill and is now known as Public Law 89-239.

State legislation will concern us with the opening of the 40th Legislative Assembly in January 1967.

PHYSICIAN'S PLACEMENT SERVICE: This office continues to give service to communities and/or medical groups seeking physicians.

U.N.D. MEDICAL SCHOOL SCHOLARSHIPS: The 1965 winners of the Association's Scholarship Prizes (totalling $500.00) offered at the School of Medicine were as follows:

Highest Average Mark in Microbiology—
C. Ellis Hageseth, Minot, N.D.

Highest Average Mark in Pathology—
David T. Purtilo, St. Paul, Minn.

Highest Average Mark in Physiology—
John R. Fischer, Minot, N.D.

Highest Average Mark in Anatomy—
Philip J. Johnson, Willmar, Minn.

Highest Average in the Work of the First Year—
Margaret Wright, Fargo, N.D.

MEDICARE: The Dependents' Medical Care Program (Medicare) commenced on December 7, 1956. Up to January 1, 1966, 11,840 claims had been processed by this office.

The total amount paid to North Dakota physicians as of December 31, 1965, amounted to $981,651.00.

Each claim for services given averages out at $82.09.

FINANCE: The goal of having one year's operating budget in reserve was maintained last year when you consider the certificates of deposit in the headquarter's office account. It is hoped that this reserve can be kept at this level, as it should be, in the interests of good business practice.

THOUHTS FOR THE FUTURE:

1. As citizens, we must take a greater interest and play a more active part in politics beginning on the local level. This is an important election year in North Dakota since we have had redistricting in our State. The Congressional elections also take place this fall.

2. Plans should be made shortly so that a positive program of health legislation will be ready for presentation to the next (40th) Legislative Assembly in January 1967.

3. The members of this Association should give serious thought, before July 1, 1966, as to the part they are to play under Medicare (P.L. 89-97) as to utilization review committees and direct billing of patients versus assignment.

ACKNOWLEDGEMENTS: Your Executive Secretary wishes to express his sincere appreciation to our President, Joseph D. Craven, M.D., for his efforts in behalf of this Association. Dr. Craven made many trips both in and out of the State on Association business.

My sincere thanks also go to those other members with whom this writer has had occasion to work this past year on committee assignments and the several other programs of the Association.

Respectfully submitted,
(Signed) Lyle A. Limond, *Executive Secretary*

REPORT OF THE CHAIRMAN OF THE COUNCIL

The First Session of the Council was held Saturday, May 1, 1965 in Grand Forks. The meeting was called to order at 10:00 A.M. by the Chairman, Dr. R. E. Mahowald. The Secretary, Dr. Keith Foster, called the roll and the following Councillors responded:

Drs.: Frank DeCesare, Ralph Mahowald, R. W. McLean, Frank Naegeli, W. R. Fox, Amos Gilsdorf, Dean Strinden, G. Christianson, Keith Foster, J. M. Van der Linde, and C. H. Peters.

Others present were: Drs. E. H. Boerth, R. D. Nierling, G. A. Dodds, Lee Christoferson, R. C. Painter, Wm. Buckingham, J. D. Craven, J. J. Moses, Tom Pederson, and Mr. Lyle Limond and Mr. Sherwood Williams.

It was moved by Dr. McLean, seconded by Dr. Strinden, that the reading of the minutes of the Council Meeting of December 12, 1964 be dispensed with, and that they be accepted as printed in the Council Agenda. Motion passed.

Dr. Mahowald advised that the budget for 1965 was approved at the December 1964 meeting of the Council. Dr. Nierling, Treasurer, gave a brief summary of the financial condition of the Association, and stated that he did not think it would be necessary to increase the dues for the coming year.

The next item on the Agenda, MEDICARE negotiations with ODMC was thoroughly explained by Dr. Peters. He read a letter from General Peatfield to which was attached a brief analysis of the proposed schedule for six services. Dr. Peters advised that when he met with the General on this matter, the General agreed to renew our present contract for one year to give time for the Medical Economics Committee to meet and discuss this fee schedule. At that time they asked for four items to be readjusted and in the letter they had increased this to six items. Dr. Peters suggested two or three things the Council could do at this time; namely, to authorize Mr. Limond and the President, or himself, as they wish, to sign a renewal of the present contract pending negotiations; to request the Medical Economics Committee to review the schedule this summer and make a decision as to whether they want to continue under the present contract, renegotiate, or give up this entire program. The Council should advise the Medical Economics Committee as to their feeling on the Blue Shield Plan B or whether they wish to stick to the old maximum allowance, or renegotiate these six items.

Dr. Strinden moved that the President of the North Dakota State Medical Association, or his self-designated representative, sign renegotiating contracts and that the President shall be responsible for the signing of all future contracts with the ODMC. Dr. DeCesare seconded the motion and motion passed.

Motion was made by Dr. Peters, seconded by Dr. Strinden, that the Committee on Medical Economics be instructed to review the fee schedules within the next six months. Motion passed.

Dr. Mahowald reviewed the action taken by the Council on MEDICARE contracts; namely, authorizing the signing of the present contract; recommending to the Committee on Medical Economics to meet at an early date to study the fee schedule plan for renegotiating a new contract; advising the Committee that Dr. Peters would be available to meet with them. There being no further recommendations, the subject is closed.

Dr. Pederson, Delegate to AMA, appeared before the Council to discuss the candidacy of Dr. Willard Wright for President-Elect to the American Medical Association. After discussion, Dr. Strinden moved that the Council authorize the Executive Secretary to allot an expenditure up to $1,000 for the purpose of furthering the campaign of Dr. Willard Wright as President-Elect of the AMA. Dr. Naegeli seconded this motion. Motion passed.

There followed a discussion of House Bill HR 7—39th Legislative Assembly. This is a Resolution regarding a composite board of medical doctors and osteopaths for examination and licensure. The Speaker of the House appointed a Committee consisting of two members of the House of Representatives, two members of the Board of Medical Examiners, and two members of the Board of Osteopathic Examiners. This committee is to study the feasibility of a composite board of M.D.'s and D.O.'s. Recommendations and any proposed legislation are to be submitted to the 40th Legislative Assembly. This item will be brought before the House of Delegates meeting on Saturday afternoon and then be referred to the Resolutions Committee for action.

Mr. Limond read a letter from Medico, a service of CARE, requesting a mailing list of the doctors in North Dakota, which list could be used to seek funds from the North Dakota doctors. It was decided that the State Association should not be involved in this.

Dr. Mahowald discussed a letter from the Safety Responsibility Division of the State Highway Department, asking for an appointment of a Medical Advisory

Committee to give competent medical advice concerning physical and mental problems of persons operating motor vehicles in North Dakota. Dr. Gilsdorf moved that the Council recommend that such a Committee be appointed by the President; details and number to be decided upon by the President. Dr. DeCesare seconded the motion; motion passed.

The next item on the agenda, a Resolution from the Whatcom County Medical Society of Washington State, was brought up for discussion. The AMA Field Representative, Mr. Sherwood Williams, explained this resolution to the Council. He stated that this is asking for a plan by which individual members of the AMA can vote by ballot on all decisions of importance concerning common interest and official policy. He stated that realistically this was not a good idea because every important question that came up would have to be sent out in the form of a questionnaire to all members. It has been proved that only about thirty percent of the physicians are active and would read and answer this questionnaire.

Dr. McLean moved, and Dr. Foster seconded, that this item be tabled. Motion passed.

Recess 12:00 NOON. To reconvene at 1:15 P.M.

Dr. Ralph Mahowald, Chairman of the Council, called the meeting to order at 1:15 P.M.

Dr. Mahowald brought up the subject of a $50.00 prize given by the Association for the Science Fair, for an outstanding student in the State of North Dakota in the Biological Sciences. The Council received a letter of appreciation from the Director of the Science Fair, expressing the hope that we would continue this $50.00 award. The Council also received a letter from a youngster from Larimore to the effect that the Larimore Science Club would appreciate a donation. After discussion, Dr. Gilsdorf moved that the Council instruct the Executive Secretary to communicate with the Larimore student and explain to him the reason it would be impossible for the State Association to donate anything to a local community club such as theirs and suggesting that he could refer this to the local District Medical Society. Motion passed.

Dr. Gilsdorf then suggested that the Council authorize an annual contribution to the State Science Fair for a prize to an individual in Biological Sciences, or its application to the medical field. After some discussion, Dr. DeCesare moved that the Council authorize a contribution of $100.00 for the Science Fair to be used for an award, or awards, consisting of a minimum of $50.00 each, to an individual, or individuals, in Biological Sciences. Dr. Strinden seconded this motion and motion passed.

Dr. Peters stated that Dr. Amos, Director of the State Health Department, had presented him with a pamphlet on "How to Get Good Medical Care." Dr. Amos had read this over and thought the State Health Department might want to distribute this to patients or citizens in North Dakota. However, he asked that it be presented to the Council as he thought the first paragraph might be controversial. Dr. Peters moved that the Council refer this to the Committee on Public Relations with the instructions to delve into this and decide whether they wish to present this or not. Dr. Strinden seconded this motion and motion passed.

Dr. Mahowald then introduced Dr. R. J. Ulmer of COMPACT. Dr. Ulmer briefly outlined the work of COMPACT during the past year and asked that the Association consider the suggestion of having the President appoint members to the COMPACT Board in North Dakota. He then introduced Dr. Hemingsgaard of Oregon, Director of AMPAC, who outlined briefly the plans other states are using of combined billing for State COMPACT and AMPAC dues. He also suggested a plan of giving funds for State PAC committees through the Legislative Committee.

Dr. Strinden moved that discussion and action of the COMPACT suggestions be postponed until after the House of Delegates meeting on Sunday. Dr. DeCesare seconded this, and motion passed.

Dr. Mahowald asked for action of the Council on the following Resolution:

RESOLUTION

WHEREAS, a two-day Speech Training Seminar for physicians and auxiliary members was conducted in April, 1965, through the good offices of the Speech Training Service of Smith Kline & French Laboratories; and,

WHEREAS, the Seminar was sponsored by the Committee on Public Relations, at the request of the Council, as a vital part of the Association's continued efforts to tell its story to the people of North Dakota with trained and articulate speakers; and,

WHEREAS, we believe that the intent of the Council in requesting such a Seminar was surpassed through the excellence of the instruction given by the staff of Smith Kline & French Laboratories; NOW, THEREFORE,

BE IT RESOLVED, that the Council congratulate Smith Kline & French Laboratories, and especially Robert Haakenson, Ph.D., Community Relations Manager, for their high-minded service to this Association in providing a Speech Training Seminar in our State; and,

BE IT FURTHER RESOLVED, that a copy of this resolution be directed to Dr. Haakenson and the other staff of Smith Kline & French Laboratories, and that the Committee on Public Relations be encouraged to sponsor additional Seminars of this nature in the future.

Dr. Peters moved the adoption of this Resolution. Dr. DeCesare seconded this motion, and Resolution was adopted.

Dr. Wright appeared before the Council to thank them for their expression of confidence in him, in regard to his candidacy for President-Elect of the AMA. Dr. Wright stated that he would try to live up to their confidence.

There being no further business, the meeting of the Council was adjourned at 2:00 P.M. to reconvene on Sunday, May 2, 1965, after the House of Delegates meeting.

SECOND SESSION

Sunday, May 2, 1965—Grand Forks, North Dakota

Chairman Dr. Mahowald called the meeting to order at 5:15 P.M. on May 2, 1965 in Grand Forks, North Dakota.

The following doctors responded to roll call: Drs. Dean Strinden, G. Christianson, Ralph Mahowald, Frank Naegeli, R. W. McLean, Keith Foster, R. B. Tudor, F. A. DeCesare, W. R. Fox, J. M. Van der Linde and Dr. A. R. Gilsdorf and Dr. G. A. Dodds.

Dr. Mahowald called for election of officers. The following Councillors were elected to office unanimously: Dr. Mahowald as Chairman, Dr. Strinden as Vice-Chairman, and Dr. Foster as Secretary. A discussion was instituted on the mechanics of setting up the budget and how this is controlled and cared for.

Dr. Mahowald then asked the Speaker of the House, Dr. Lee Christoferson, for instructions sent to the Councillors by the House of Delegates.

Speaker Christoferson stated that the formulation of next year's meeting would take precedence over all other items and offered a suggestion for the Council's consideration on how this meeting should be held. He suggested that the business meeting be held Friday morning; Scientific session on Friday afternoon; then it could be announced that the reference committees would hold open hearings at a certain time and place on Saturday, to give the members a chance to express their opinions on certain items. The Scientific program could be held on Friday afternoon and on Saturday morning—and the reference committees' discussions could be perhaps from three to five on Saturday afternoon. The Scientific Session could then be held again on Sunday morning and the House of Delegates meet from 2:00 o'clock Sunday afternoon until 5:00 o'clock. The dates for the 1966 annual meeting were set for April 29 and 30, and May 1, at Fargo, North Dakota.

Considerable discussion followed this suggestion. Dr. Mahowald asked Mr. Limond to procure a program format from the Montana and Minnesota Associations by June 15th. Dr. Mahowald then suggested that the Executive Secretary and the Chairman of the Council set up some format for next year's meeting and send this to Dr. Christoferson, Speaker of the House.

Speaker Christoferson then brought up the request by the Woman's Auxiliary of having their dues enclosed in the billing of the Association dues to their husbands. The House of Delegates approved this in principle and asked that it be referred to the Council for action. After a general discussion, Dr. Foster moved that the Council recommend to the individual district society treasurer that a composite bill be itemized, and the treasurer could implement this to their own discretion. Dr. DeCesare seconded the motion and motion passed.

Speaker Christoferson then brought up the recommendation made by the House, to be referred to the Council, that the President-Elect of the North Dakota State Medical Association be given an allowance of up to $600.00 for travel expense. Dr. DeCesare moved that the Council allocate an amount up to $400.00 for the expenditures of the President-Elect for the ensuing year. Dr. Strinden seconded the motion. Motion passed.

Speaker Christoferson then brought up the recommendation by the House that the Chairman of the Council, with the approval of the Councillors, appoint the Board members for COMPACT. Dr. Ulmer suggested that the Council appoint the Board members in December and that the Board could consist of seven members, six of whom would be physicians and select one of the ladies to serve on this Board. He also suggested that, in the future, the activities could be enlarged to encourage other medical people, such as dentists or pharmacists, to serve on the Board. Dr. Strinden suggested that the Chairman of the Council contact Dr. Ulmer before December for suggestions as to Board members.

Dr. Strinden moved that the Secretary write to Dr. Peters a letter of thanks for the fine work he did while a Councillor. Dr. McLean seconded the motion. Motion passed.

There being no further business, motion passed for adjournment. Adjournment at 6:15 P.M.

INTERIM MEETING

Saturday, December 11, 1965, Fargo, North Dakota

The meeting was called to order by the Chairman, Dr. Mahowald, at 10:00 A.M., with a quorum present. Councillors present were: Drs. Ralph Mahowald, R. W. McLean, R. B. Tudor, Keith Foster, W. R. Fox, F. D. Naegeli, Dean Strinden and G. Alfred Dodds. Absent were: Drs. G. Christianson, F. A. DeCesare and J. M. Van der Linde.

Others present were: Drs. Glenn Toomey, C. H. Peters, Lee Christoferson, R. D. Nierling, T. E. Pederson, R. C. Painter, V. J. Fischer, O. V. Lindelow, W. M. Buckingham, J. D. Craven, P. L. Owens, T. L. Donat and J. R. Amos. Also present were Mr. Howard Brower, Mr. Lyle A. Limond, Myrtle Kohler and Margaret Fremming.

The first item on the agenda was the introduction of Mr. Howard Brower of the State Medical Society of Wisconsin. Mr. Brower discussed Public Law 89-97 in detail and invited questions from the members of the Council. He stated that should the Government designate an area-wide carrier for the implementation of P.L. 89-97, it was his hope that the State Medical Society of Wisconsin be endorsed as such a carrier since they are fully equipped to administer Part B of the Law.

A general discussion followed with questions being directed to Mr. Brower.

Mr. Limond next reviewed the proposed Budget for 1966. A discussion followed covering the following points: 1) The question was raised if the C.D.'s now held by the Office of Executive Secretary should go into the regular account of the Treasurer. It was the decision that they be left as is, since they are regularly accounted for. 2) Dr. Nierling requested that he be advised when interest payments on the C.D.'s are received. 3) Dr. Nierling was asked to investigate the feasibility of putting excess funds (dues payments) into C.D.'s during the months between requests from the Office of Executive Secretary (made three times yearly) for a portion of the budget.

Dr. Tudor made the motion that the finances and audit be handled by one auditing firm, the mechanics to be worked out by the Executive Committee of the Council. Seconded by Dr. Dean Strinden and carried.

Dr. Strinden made the motion that the full time employees of the North Dakota State Medical Association be covered by Blue Cross–Blue Shield, single coverage. Seconded by Dr. McLean and carried. (This represents an increased expenditure of $321.60 yearly for Blue Shield and Blue Cross coverage which does not appear on the approved Budget and will be taken out of the Miscellaneous Budget, but to be incorporated under a fixed heading for the year 1967).

Dr. Dodds presented the retirement insurance plan regarding Mr. Limond. He then moved the Council accept and pay for Plan No. 1 and Blue Cross–Blue Shield, as presented. Seconded by Dr. Tudor. A discussion followed and the motion carried. (This item of increased budgeting will not appear under Insurance and is to be taken from the Miscellaneous Budget for 1966, but will properly appear under Insurance as a separate item in the 1967 Budget. The specific figure for this, the first year, is $884.80.)

Dr. Tudor moved the item of "Committee on Public Relations" be changed to read "Office of Assistant Executive Secretary and the Director of Public Information and Education," the budgeting cost to remain the same. Seconded by Dr. Strinden and carried.

Dr. Tudor made the motion that the budget for 1966 be accepted as presented with the recommended change. Seconded by Dr. Naegeli and carried.

T. E. Pederson, M.D., Delegate to the AMA, gave a brief summary of the recent meetings he had attended. He advised the Council that all possible support had been given to the campaign of W. A. Wright, M.D., for President-Elect of the AMA, although the efforts had not been successful. He recommended that North Dakota should have a task force to represent the several committees in various Government issues as they come up. A recommendation had been made that AMA dues for 1967 be increased $25.00 per year, the recommendation to be voted on in June of 1966. He explained that a raise in AMA dues had been recommended because of new programs being implemented, including research. He touched briefly on AMPAC, stating that 30 states bill for dues along with their regular billing, and he felt that although North Dakota has made a good showing, the Association could do better. He made the suggestion that excess funds held by the various District Medical Societies could be donated to AMA-ERF. He requested guidance from the Council as to his participation in future meetings.

The next item on the agenda was the selection of Board of Directors for COMPACT. In accordance with a motion made and passed by the Reference Committee, considering reports of the Committee on Medical Economics, (House of Delegates) "the Chairman of the Council, with the approval of the Councillors, appoint the board members of COMPACT." Dr. Strinden made the motion that the Councillors submit a slate of names to the Chairman, Dr. Mahowald, for appointment to the Board of Directors. Seconded by Dr. McLean and carried. The following names were submitted: Western District—R. S. Larson, M.D., Velva; P. O. Dahl, M.D., Bismarck; and W. C. Hanewald, M.D., Dickinson. Eastern District—R. J. Ulmer, M.D., Fargo (Chairman Pro Tem until election held by members of the Board); J. N. Elsworth, M.D., Jamestown; W. T. Powers, M.D., Grand Forks; and G. Christianson, M.D., Valley City. Dr. Tudor made the motion that the seven physicians named above be appointed as Board members of COMPACT. Seconded by Dr. Strinden and carried unanimously. Mrs. M. A. K. Lommen, President, Woman's Auxiliary to the North Dakota State Medical Association is to be contacted for her recommendation of an Auxiliary member to serve on the Board of COMPACT.

The format for the 1966 annual meeting, to be held in Fargo, was next discussed. The tentative schedule was approved with the exception of the Reference Committee Hearings meeting times. At the recommendation of Lee Christoferson, M.D., the Speaker of the House of Delegates, the Reference Committees will meet Saturday, April 30, 1966 from 9:00 to 10:30 A.M., and immediately following the last speaker for the day, at 4:15 P.M., until work is completed. Rooms for meetings to be arranged at the Town House.

The Council was in agreement that the 1967 annual meeting be held in Bismarck.

A discussion followed to review the presentation made by Mr. Brower of the Wisconsin State Medical Association. It was stated that a letter from the Council had been directed to Blue Shield designating them as the intermediary for the North Dakota State Medical Association for the implementation of Public Law 89-97, and they have filed a letter of intent with the Government. A decision by the Government is to be made by the first of the year, as to carriers, and it was the consensus of the Council that a special meeting could be held if Blue Shield is not appointed. The motion was made by Dr. McLean that the matter be tabled at this time. Motion seconded by Dr. Tudor and carried.

The next item of business was a slate of nominees to be selected for submission to the Governor for appointment to the State Health Council. The following names were submitted by the various Councillors: Edmund Vinje, M.D., Hazen; P. R. Gregware, M.D., Bismarck; C. M. Lund, M.D., Williston, and Keith Vandergon, M.D., Grand Forks. Dr. McLean moved that these physicians be contacted for their approval to have their name submitted and to ascertain if they would accept if the Governor should appoint one of the four. Seconded by Dr. Strinden and carried. (Dr. P. Roy Gregware was subsequently appointed by the Governor.)

Dr. O. V. Lindelow, Chairman, Committee on Medical Economics, next addressed the Council and reviewed the actions of the Committee at their November 13 and December 10, 1965 meetings. He stated that the motion made at the November 13th meeting "mileage from the city limits to the patient is at .2 units per mile, one way" had been acceptable to Mr. Ovre of the Public Welfare Board. The decision on another motion "that all charges to the Public Welfare Board be at the usual and customary fees charged anyone," will be forthcoming after a meeting of the Board to be held shortly. At the December 10th meeting, it was the decision of the Committee to use the usual and customary fees to negotiate with all of the Federal Agencies. The motion was made that the figures to be given to all Federal Agencies for negotiation, based on the 1958 schedule, plus the 1964 schedule, be: Medical, 4.50; Surgery, 4.50; X-ray, 5.00; and Laboratory, 5.00.

Dr. J. D. Craven, President, North Dakota State Medical Association, made a short address to the members assembled, at this time. He thanked the Councillors and Officers for their cooperation and hard work and stated that he felt the Association is in good hands. It was his feeling that all physicians must unite to take steps to prevent any extension of the Medicare Act, and to view with suspicion all actions of Congress regarding legislation in Health Care. He then read a communication from the Minnesota State Medical Association concerning a series of 30 educational television programs for physicians to be carried regularly, in the course of the next year, over the three educational television outlets in Minnesota, and perhaps to include the TV station in Fargo as an outlet. Dr. Strinden made the motion that the communications be turned over to the First District Society for their consideration. The motion was seconded by Dr. Tudor and carried.

Mr. Limond was instructed to inform Mr. Brunn of the above, with a copy of the letter directed to Dr. Schneider, President, First District.

T. L. Donat, M.D., Radiologist, Fargo, North Dakota, next appeared before the Council requesting some action from it in its capacity as Grievance Committee for the Association. He stated that the issue had been presented to the First District Medical Society and that the problem had been resolved by them, in Dr. Donat's favor. However, he wished to carry the matter further and had, therefore, brought the matter to the Council. It was the opinion of the Chairman, Dr. Mahowald, that the presentation should be considered only as an informational matter. It was his feeling that Dr. Donat should have requested the First District Medical Society to forward to the Council all information pertaining to the matter and the subsequent action. Dr. Dodds was asked to request the First District Grievance Committee to send to the Council copies of all action, correspondence and replies, if any.

Dr. James R. Amos, State Health Officer, was next introduced to the Council. He briefly explained the responsibilities of the State Health Council, stating that it meets at least twice a year and usually four times. It is the policy making body of the Health Department and has the ultimate authority. A member appointed to this Council can serve innumerable terms. He presented, for the consideration of the Council, a request for the endorsement of a program of Home Health Services. It was noted that approval had previously been granted by the Council for a pilot study to be conducted in the First District Medical Society (Fargo) and later reports indicated that this had been successful. After considerable discussion the motion was made by Dr. Fox and seconded by Dr. Strinden that the proposal be tabled until further study could be made. Carried.

Motion made by Dr. McLean for adjournment. Adjournment: 5:20 P.M.

Respectfully submitted,
(Signed) R. E. MAHOWALD, M.D.,
Chairman of the Council

REPORTS OF COUNCILLORS

First District

During the last fiscal year, March 1965 through February 1966, the First District Medical Society held eight meetings. These meetings were all held at the Oak Manor Motor Lodge in Fargo. The March meeting was held on the 29th of the month. In the absence of the President, the meeting was called to order by the Vice-President, Dr. Blaine Amidon. The scientific portion of the program was carried out first. Dr. Geston introduced the speaker of the evening, Dr. Dale Liechty of the Department of Surgery of the University of Iowa Medical School. His topic was "Diagnosis and Treatment of Disease of the Adrenal Gland." Discussion followed the presentation of a very interesting paper. After the Scientific Program the minutes of the Board of Directors of the First District and of the last meeting were read and approved. The application of Dr. G. Obert was read for the second time and the application for membership of Dr. Leonard Levine was read for the third time. Dr. Levine was then elected unanimously into the membership of the First District Medical Society. At this meeting recommendations were brought up to the Society that a committee be established within the First District to clear all medical talks by physicians before lay groups. This elicited a considerable amount of discussion both pro and con by members of the Society. It was finally moved that the Public Relations Committee of the First District Medical Society be utilized to clear all requests for speakers and appearances on radio and television. Dr. Amidon concluded the meeting by announcing that the April meeting was a regular business meeting and that Delegates from the State Society were to report at the next meeting of business on any matters that were to be brought up before the State Society meeting in May. The meeting adjourned.

The next regular meeting of the First District Medical Society was held on Monday, April 26, 1965. The meeting was called to order by the President, Dr. J. F. Schneider. In the absence of the Secretary, Dr. Robert Ulmer acted as Secretary for the meeting. The minutes of the previous meeting were read and approved. Dr. Burgess Gorden from Chicago was introduced to those in attendance. Dr. Gorden was a physician in residence for three days at the Fargo VA Hospital. The third membership application of Dr. G. Obert was read and after distribution of secret ballots he was unanimously elected to membership. Committee reports were asked for and Dr. Fercho, as Chairman of the Public Relations Committee, reported that his committee had met and drawn up ground rules to be followed by the members of the Society with regards to public appearances. Dr. Macaulay announced at this meeting that the State Medical Association meeting would be held in Fargo in 1966. He requested that any member who had suggestions for the scientific program contact him or some other member of the State Committee so that work may be begun on lining up next years program. Dr. Gillam announced at this meeting that the Cancer Society had changed its policy and would give no further direct financial aid to cancer patients. He stated that they have wheelchairs available for patients on application. Dr. Traynor, as a member of the program committee, requested permission for his committee to accept the offer of drug companies when given, to sponsor speakers for the First District Medical Society and he so moved. There was considerable discussion pro and con of this particular proposal. Dr. Traynor's motion was finally voted on and carried by a show of hands. The meeting then was turned to the problem of instruction of the delegates to the state meeting which was to be held in Grand Forks the following week. One of the items that would be brought up would be the proposed change in the election of Councillors for the district. Dr. Dodds pointed out that a resolution was to be introduced from the Grand Forks Society changing the constitution of the State Association to provide for election of Councillors by the District rather than by the State House of Delegates. He advised no change in the present setup. Dr. Gillam moved that our delegates vote against the proposed resolution and that the District Society propose more than one candidate to the state nominating committee. This motion was seconded by Dr. Christoferson, but failed to pass. The motion that did was one moved by Dr. Sessums that the delegates be instructed to support the resolution providing for the election of the Council by the districts at home. Several other matters came up at this time as to instruction of delegates such as a bill providing for a committee of physicians, osteopaths, chiropractors and legislators to study the problem of licensure with the goal in mind of creating one board of licensure. Also brought up was a point from the Nurses Association as to what medication and routes of administration a nurse might be authorized to administer. Dr. Ulmer brought up the discussion of the proposed medicare legislation which had passed the House of Representatives in Washington. The meeting was adjourned at 10:00 P.M.

Since there is no May meeting because of the State Medical Association meeting, the next meeting of the First District Society was held on September 27, 1965. The meeting was called to order by the President, Dr. J. F. Schneider. At this meeting, Dr. J. D. Craven, of Williston, President of the State Medical Association was introduced by Dr. Schneider. He spoke briefly to the membership regarding the present status of medicine and its relation to the federal government. Mr. Lyle Limond, Executive Secretary of the North Dakota State Medical Association was introduced and also spoke to the membership. A guest was introduced by Dr. Robert Ulmer. The guest was Mr. James Rosevear of AMPAC. Mr. Rosevear was the regional representative of AMPAC with his offices in Minneapolis. He offered his services and the services of his office to our society at any time. The membership applications of Dr. Bruce J. Bart and Dr. Richard Olafson were read for the first time. Dr. Fercho reported for the Public Relations Committee. Dr. Landa reported for Dr. Macaulay, soliciting suggestions and topics for the State meeting which would be held in Fargo next year. Dr. Ulmer then gave a comprehensive report for the delegates from the last State Medical meeting. He discussed the matter of collection of dues for the Ladies Auxiliary. The passed resolution allowed local societies to implement billing of their own wishes. His second point was that of the North Dakota State Medical Association setting a committee to meet with the Hospital Association regarding state planning for hospitals. 3) Tetanus immunization weeks to be established at the local level. 4) In 1966 Councillors will be selected from a list of nominees submitted by the local societies. 5) The North Dakota State Medical Association advocates law in North Dakota for driver fitness on medical basis. 6) An orientation program for new doctors arriving in the State would be established. 7) Recommendation for collection of dues to AMPAC and COMPACT. 8) The Chairman of the Council of the State Society will appoint the Board of Directors of AMPAC and COMPACT. 9) A new abortion law will be proposed. 10) Went on record opposing social security coverages for physicians. 11) The number of delegates in the house to be determined by the number of paid up members in the local societies. Under new business, Dr. Houghton recommended that the local societies go on record advocating that the Blue Shield Board become the negotiating board for the medicare program. This was moved and passed. The meeting was adjourned at 9:10 P.M.

The next regular meeting of the First District Medical Society was held on October 25, 1965. The meeting was called to order by the President, Dr. J. F. Schneider. Dr. Robert Ivers, Program Committee, introduced the speaker of the evening, Dr. Ralph Williams, Jr., of the University of Minnesota Medical School. Dr. Williams spoke on the subject of arthritis and his talk was sponsored by the North Dakota Chapter of the Arthritis Foundation. The minutes of the September meeting were read and approved. Membership applications of Dr. Bruce Bart and Dr. Richard Olafson were read for the second time. The meeting was adjourned at 9:00 P.M.

The next regular meeting was held on November 29, 1965, called to order by the President, Dr. Schneider. Minutes of the previous meeting were read and approved. The application of Dr. J. E. Nord was read for the first time and the applications of Dr. Richard Olafson and Dr. Bruce Bart were read for the third time. Both men were elected to membership unanimously in the First District Medical Society. A letter from the President of the Woman's Auxiliary was read at this meeting which was directed to the State Medical Association relating to the giving of contributions to the AMA-ERF, to funnel them through the State Auxiliary so that they might receive credit for it. The following members were elected to the nominating committee: Drs. Calvin Fercho, Donald Barnard and Robert Ulmer. The scientific program of this meeting was presented by Dr. Louis Tobin from the University of Minnesota Medical School. He spoke on the role of the juxtaglomerular apparatus in hypertension. The meeting was adjourned after the presentation.

The next regular meeting was held on December 20, 1965, called to order by the President. The minutes of the previous meeting were read and approved. The application of Dr. Nord was read for the second time. Dr. Ulmer reported as Chairman of the Nominating Committee and proposed the following slate of officers for the coming year: President, Dr. Blaine Amidon; Vice-President, Dr. William Webster; Secretary-Treasurer, Dr. Henry Norum; Board of Censors, Dr. Bernard Mazur; Delegates to the House of Delegates of the State Medical Association, Drs. Henry Norum, M. H. Poindexter, A. C. Burt, Roy Kulland, Paul Beithon, B. F. Amidon and R. J. Ulmer; Alternates to the State Medical Association House of Delegates: Drs. John Gillam, Neill Goltz, Robert Gaebe, Calvin Fercho, E. R. Wasemiller, James Houghton and Neil Williams. Dr. Gillam issued a complaint at this time about the speaker appearing on the program not being the first presentation of the agenda. It was pointed out that this was done at all meetings except the November meeting. On this occasion the projector was not available and the regular business meeting progressed until the projector was obtained. The meeting adjourned at 8:10 P.M.

The next meeting of the First District Medical Society was held on January 31, 1966. The meeting was called to order by the new President, Dr. Blaine Amidon, at 8:00 P.M. The minutes of the previous meeting were read and approved. The application of Dr. Ross Halliday and Dr. Ann Schutt were read for the first time. The application of Dr. Nord was read for the third time and he was unanimously elected to membership. The speaker of the evening was Dr. M. K. Burbank who is consultant in medicine, Section of Vascular Diseases of the Mayo Clinic and he spoke on the diagnosis of pulmonary embolic disease. At this meeting a moment of silence was observed in the memory of one of our members, Dr. George Ivers, who died on January 26, 1966. It was also discussed at this meeting that the February meeting would be held at the usual time on the last Monday of the month and that no change would be necessary as had been anticipated. It was also voted to change the April meeting from the 25th of April to the 18th because of the fact that the State Medical Association meeting would be in Fargo starting April 29th. It was announced that Drs. Ulmer, Fercho and Story would be in charge of local arrangements for the State Medical Meeting. Dr. Ulmer discussed some of the problems involved in planning for the meeting. Dr. Amidon announced at this time that most of the committee assignments had been made, but that the membership should give serious thought to just how the grievance committee should be used. The meeting adjourned at 9:10 P.M.

The last meeting of the First District Medical Society was held on February 28, 1966. The meeting was called to order by the President, Dr. Blaine Amidon. The minutes of the January meeting were read and approved. The application of Dr. Robert Leegard was read for the first time. The applications of Dr. Ross Halliday and Dr. Ann Schutt were read for the second time. It was announced by the Secretary that the AMA proposes to increase dues beginning in 1967 from $45.00 to $70.00. This increase awaits the final approval of the House of Delegates meeting in June, 1966. Dr. Ulmer, Chairman of the Arrangements committee for the coming state meeting, reported briefly on plans which have already been formulated. Dr. Houghton reported on the preliminary meeting of interested individuals on the government plan to establish treatment centers for stroke, heart disease and cancer which was held in Fargo on February 26th. Another suggestion arose from the meeting concerning the duties of the grievance committee which requested that a liaison committee with the local bar association be asked to inquire of local attorneys their plans to change methods of gaining access to medical records. Discussion was held regarding the closing of doctors' offices during the annual state medical meeting in Fargo and having a notice of said action placed in the newspapers. The scientific program consisted of a very interesting paper presented by Dr. Hubert A. Carbone, Psychiatrist, Superintendent of the State Hospital in Jamestown. His paper was entitled "Psychotherapy in Internal Medicine." A very lively discussion followed the talk. The meeting adjourned at 9:10 P.M.

Respectfully submitted,
(Signed) F. A. DeCesare, M.D.,
Councillor, First District

Second District

The Devils Lake District Medical Society held nine meetings during the fiscal year from March 1965 through February 1966. The attendance at the meetings during 1965 was excellent except on two or three occasions when the weather was bad and it was difficult for members to drive great distances. The members from Bottineau are to be commended for their excellent attendance, especially in view of the distance of 110 miles required to be present at each meeting.

Five new members were presented for membership in our Society and approved, namely Dr. Rodney Slonim and Dr. Bernie Zitsow and Dr. Klassen of Devils Lake, Dr. Arnold J. Overland of Rolla and Dr. Antonio Mimay of Maddock. The present staff of officers were elected in January and will hold office during the coming year. They are listed as follows:

President:

DR. DAVID A. RINN	Cando

Vice-President:

DR. LYLE HILLMAN	Rugby

Secretary-Treasurer:

DR. LOUIS F. PINE	Devils Lake

Delegates:

DR. G. A. HILTS	Cando
DR. R. D. McBANE	Devils Lake
DR. C. ROBERT MILLER	Bottineau

Alternate Delegates:

DR. J. W. LIND	Bottineau
DR. S. J. COOK	Rolette
DR. A. NEUENSCHWANDER	Rolla

Censors:

DR. E. J. SCHWINGHAMER	New Rockford
DR. D. G. McINTYRE	Rugby
DR. J. TERLECKI	Minnewaukan

The Delegates to the State Association were nominated as Corporation Members to the North Dakota Physicians Service. Dr. L. F. Pine, Devils Lake, was re-elected as Board Member to the North Dakota Physicians Service.

The majority of the meetings of the Devils Lake District Medical Society were held at the Ranch at Devils Lake, North Dakota, with one meeting being held at Andrew's Steak House at Rugby and one meeting at Timber-Wolf-Up-Lodge, Lake Metigoshe.

March 4, 1965, Dr. Robert Fontana, Section of Thoracic Diseases, Mayo Clinic, spoke on "Pulmonary Cancer in General" and was very well received. The business meeting consisted of passing on the application of Dr. Leonard Klassen of Devils Lake. Communications were read regarding the selection of councillors and one from the North Dakota Physicians Service regarding the election of members to the Corporation meeting. Dr. Lazareck brought up the fact that frequently no doctors were covering the First Aid Station during the session of the Legislature and he moved that each District evolve a proportionate representation according to the number of doctors in their District and be responsible for so many days of the Legislative Session. Discussion regarding the type of meetings we should have took place. A motion was finally made that we continue the same as in the past—namely, five or six scientific programs with three purely non-scientific sessions.

April 8, 1965: No scientific speaker was present at this meeting. It was purely a business meeting prior to the annual North Dakota State Medical Association meeting. Dr. Longmire introduced the subject of a glaucoma survey clinic to be held in Devils Lake during the spring. A request was presented for Dr. McLaughlin, a psychiatrist, to be present at one of our meetings to explain to the Society the North Dakota Mental Health Clinic Program. It was agreed that this should be done at some future time. No further discussion took place and the meeting was adjourned.

May 6, 1965: Meeting was held at Andrew's Steak House at Rugby and was a post-convention meeting to discuss the business which took place at the annual medical meeting. Five clinical clerks from the North Dakota Medical School, attending Rugby, Bottineau and Devils Lake Hospitals, were guests of the Medical Society. Dr. Glenn Toomey, President-Elect of the State Medical Association, was recognized by the meeting and gave very thought provoking remarks directed to the medical clerks. Dr. Fox gave a report of the previous meeting of the Council of the North Dakota Medical Association. Dr. Hilts gave an interesting report on the recent meeting of the House of Delegates of the Medical Association. Letters from Dr. Amos were read concerning the polio immunization programs.

September 2, 1965: Meeting was held at Timber-Wolf-Up-Lodge, Milligan Manor, Lake Metigoshe, under the auspices of the Bottineau group in a combined meeting of physicians and their wives. No business was conducted at this meeting being purely a social meeting.

October 7, 1965: Speaker for the evening was Dr. Cornatzer, University of North Dakota. He discussed the various liver enzymes and their relationship to myocardial infarctions. A discussion also took place regarding the cholesterol problem. A short business meeting was held and four applications were presented for membership and accepted.

November 4, 1965: Guest speaker for the evening was Dr. Gozum, Minot, who spoke on "Tumors of the Head and Neck." Following the dinner, a business meeting was held. A communication from the office of the State Secretary was read stating that the dues for the North Dakota State Medical Association would remain at $100 and the American Medical Association would remain at $45. Consensus of the meeting was that the dues for the District Society is to remain at $10. Discussion took place regarding polio clinics and it was decided that we should adhere to the State Public Health regulations and advice. Discussion took place regarding the Mental Health Unit programs. It was felt that at this time all efforts should be made to maintain adequate personnel at our State Hospital and attempt to achieve greater success with this unit and simply use pilot units of the Mental Health Clinic as a study project. Discussion took place regarding Blue Shield and its role as an Intermediary in the Medicare government program. It was decided that the Blue Shield representative from our Society use his considered judgment in handling any discussion regarding this problem. The treasurer's report was given showing the presence of adequate funds in the checking account and in the Savings and Loan Association.

December 2, 1965: The speaker was Dr. J. J. McLeod of the Grand Forks Clinic speaking on the topic, "Congenital anomalies of the Lower Extremities and Methods of Treatment." A routine business meeting was held and no new problems were brought up.

January 6, 1966: Program speaker for the evening was

Dr. Joseph Craven, President of the State Medical Association. Also in attendance were past presidents Dr. Amos Gilsdorf and Dr. J. C. Fawcett. Speakers were introduced by Dr. Glenn W. Toomey, President-Elect of the State Medical Association. No business meeting was held at this time.

February 3, 1966: Speaker for the evening was Dr. C. A. Hamilton of the Quain and Ramstad Clinic, Bismarck, whose topic was "Office Screening for Surgical Heart Disease." Following this, dinner was served and a business meeting was held. Dr. Fox presented the Councillor's report, discussing the budget, the report of Mr. Brower of the Wisconsin Medical Association, a report of Dr. Pederson, Delegate to the AMA and discussion regarding the usual and customary fees and the discussion regarding the home nursing care setups and the new retirement program for Mr. Limond. Dr. L. F. Pine gave a short report on the last Blue Shield meeting. A letter was read from Dr. Ulmer of the Committee on Political Action requesting that AMPAC and COMPACT dues be enclosed with the regular medical dues. Election of officers was held. No further business being presented, the meeting was adjourned.

Respectfully submitted,
(Signed) W. R. Fox, M.D.
Councillor, Second District

Third District

The regular monthly meeting which was held in September of 1965, was held in Grafton, North Dakota by precedent previously set for the first meeting to be held in that city. There being no particular business to be taken up at this meeting, it was a very short business meeting, consisting of comments on the past state meeting, and also some comments from the alternate delegate to the AMA, namely R. C. Painter, M.D. A presentation of dermatology was presented by a member of the Winnipeg Clinic, which was very enthusiastically received by all members present. There being no further business, the meeting was adjourned.

On October 21, 1965, the Third District met in session which was held at the Bronze Boot Steak House. The first order of business that was accomplished was the reading of the minutes of the previous meeting which were approved as read. The next order of business was that of the application of three physicians who had previously been approved by the board of censors, and were returned to the society for a vote by its members. The following members were presented: Donald F. Barcome, M.D., of Grand Forks, Curtis A. Johnson, M.D., of Grand Forks, and Ronald E. Ilvedsen, M.D., of Grand Forks, as new members to the society. Upon a motion of Dr. Hamish Mann, seconded by Dr. John J. McLeod, a unanimous approval for membership was obtained. Dr. W. T. Powers then gave a report on the Blue Shield Board of Directors meeting held September 25, 1965, in Fargo, with the following notations: All physicians are to be aware of the fact that their patients 65 years and older should be encouraged to continue their Blue Cross–Blue Shield coverage until after July 1, 1966, or until such time as medicare goes into effect, as of that date. There has been considerable confusion among patients of the older age group regarding their coverage under the medicare in lieu of Blue Shield and Blue Cross. He also noted that an informational flier would be presented next spring by the Blues concerning future billings, etc. It was next noted that the committee had discussed the voluntary section of medicare (Section B) and as to whether or not Blue Shield should apply, and act as the administrative agent for same. It was recommended that the society express a specific desire that Blue Shield be the carrier for this particular district. It was also noted that the Welfare Department was desirous of some authority, and so upon a motion by Dr. Powers, and seconded, it was passed that the North Dakota Blue Shield be requested to apply as the administrative agent of Medicare within the State of North Dakota.

The next item of business was a letter from E. A. Haunz, M.D., stating that the Diabetes Week for 1965 was November 14 through November 20. Dr. Haunz raised a question of the advisability of the Third District sponsoring a Diabetic Detection Drive; this was followed by a rather lively discussion and it was determined at this time that it was too late to obtain materials for participation in the drive of 1965. It was therefore moved by Dr. Harwood, and seconded by Dr. Hill that the president appoint a committee to prepare for the drive in 1966; this was carried unanimously. Dr. McLeod then asked for the floor to discuss a relative value schedule for the State of North Dakota.

He stated that the schedule had not been revised for several years, and that the State Medical Economics Committee has been very inactive and negligent in its duty and had not met in order to bring this up-to-date. Dr. Mahowald then rose to state that there was a meeting scheduled of the Medical Economics Committee of the State of North Dakota to be held in Bismarck on November 13, 1965, and at said meeting, any society desiring to appear before the Board should make an effort to have a representation at this meeting. It was then moved by Dr. Mahowald and seconded by Dr. Haunz that the Third District Society be authorized to send three members to the meeting. The expenses of these members would be paid by the Society and that the members of this committe would be appointed by the president of the Third District Medical Society. In the absence of the President and the Vice-President, the Secretary appointed Dr. McLeod and Dr. W. W. Nelson to attend this meeting along with either the president or the secretary. The program was then turned over to John Lambie, M.D., Program Chairman, who introduced Dr. Neil Vanslow, internist at the University of Michigan at Ann Arbor, who presented the program paper "Insect Sting Hypersensitivity." The meeting adjourned at 9:45 P.M.

The Third District Medical Society met November 18, 1965, and the minutes were approved as read, of the previous meeting. The President, Dr. Helenbolt, then proceeded with the introduction of guests present and he called upon Dr. Earl Reilly of the Grand Forks Air Base to introduce several new doctors now serving at that military installation. He introduced the visitors who were in Grand Forks from the North Dakota Public Health Department, also. They were Dr. Davis and Dr. Burger. Following the introduction of these guests, the program was turned over to Dr. John Lambie who introduced Rhinehart F. Friesen, M.D., of Winnipeg, Manitoba, who presented a paper on "Amniocentesis and Intrauterine Transfusions." Following the program, the business meeting was then called to order by Dr. Helenbolt and a vote upon the admission of a new member, John Bohrod, M.D., was the first order of business. It was moved by Dr. Mann and passed, depending upon the approval of the Board of Censors, that Dr. Bohrod be approved for membership. This was seconded by Dr. Clark. The President then appointed members of the Committee for the Diabetic Detection Drive for 1966, who are as follows: Dr. Haunz, Honorary Chairman, to be assisted by Drs. Curtis Johnson, Ronald Ilvedsen, Myron Scheflo and John Bohrod. Dr. McLeod then gave a report concerning his attendance of the meeting of the Medical Economics Committee in Bismarck. He stated that this was mainly a preliminary meeting, and the main thing that was derived from this meeting was that physicians should strive to obtain their usual customary fee in dealing with Blue Shield and dependent medical cases as well as with the Welfare. He also stated that there would be another meeting in Fargo on December 10. The president, Dr. Helenbolt, then gave a report on the meeting of the Mental Health Committee and stated that as far as possible, physician referrals would be the desired way and the main way to receive patients in this facility. There was a communication from Mrs. M. A. K. Lommen, President of the State Auxiliary asking that the American Medical Association Educational Relief Fund donations be forwarded through the Auxiliary, which in our district would be Mrs. Kenneth Helenbolt, so that the state could get credit for these funds. There was also a communication from Dr. Oscar Manz from the University of North Dakota, who is the director of the North Dakota Science Fair, requesting our usual 100 dollar donation for this purpose. It was moved by Dr. Nelson, seconded and passed, that we continue our support of this project. It was then announced that the next meeting would be held December 16, 1965, at which time a Blue Shield representative would be a part of the program, and the meeting adjourned.

The December meeting was held at the Bronze Boot Steak House and was called to order at approximately 8:30 P.M. by President Kenneth S. Helenbolt, M.D. The minutes of the November meeting were read and approved. Guests and new members who were present were introduced by the President. Dr. Bohrod was introduced as a new member of the Society. Also visiting was Dr. Higgie from Michigan, North Dakota, who was invited to join our Society. There were also three representatives from the local Pharmacy Association; namely, Mr. Tom Swinglen, Mr. Robert Moe, and Mr. Jerry Default.

The first item of business was a letter that had been received from Judge Harold Haeger of the District Court, relating to the laxity in the refilling of barbituates and narcotics within this area. Judge Haeger had sent this letter to the President in order to make our Society aware of its being written so we could take any action desired. Mr. Default spoke from the Pharmacy point of view, and explained the new regulations which go into effect February 1, 1966, with regards to the dispensing of amphetamines. Next, there was a report from Blue Shield, at which time Mr. Donald Eagles, Executive Secretary of the Blue Shield and Mr. Steve Pezalla, Public Relations Officer for the Blue Shield were in attendance, and each gave short presentations on the Blue Shield Program.

The next item of business was a report from Dr. Ralph E. Mahowald, on the proceedings of the Council which met in Interim Session in the month of December, and also on the Medical Economics Committee Meeting which was held in Fargo in conjunction with the meeting of the Council. Dr. Helenbolt gave a report upon the meeting which he had attended as a representative of the Third District Medical Society with the local Mental Health Association. This association had requested our cooperation on the Mental Health and Research Program. It was moved by Dr. Clayburgh and seconded by Dr Eaton that any action that our President takes in this regard as our representative we would abide by. Dr. Harwood urged us to cooperate with the reporting of mental defectives in a program which is being initiated in the state. It was announced that the January meeting will be held at the Grand Forks Air Base, at which time election of officers would take place.

The following physicians were appointed to the Nominating Committee by the President: Chairman, Frank Hill, M.D., John Graham, M.D., L. J. Prochaska, M.D., and R. C. Painter, M.D. The Auditing Committee: Carl E. Lorentson, M.D., to be assisted by Douglas Doss, M.D. Meeting adjourned at approximately 9:45 P.M.

The January meeting of the Third District Medical Society was held at the Grand Forks Air Force Base with Major Doyce Dees, Commander of the Base Hospital acting as host. A social hour was held, followed by a buffet dinner. Following the dinner, the minutes of the December meeting were read and approved. The first order of business was presented by Dr. T. H. Harwood, Dean of the University School of Medicine, who reported that he received a letter from the Lederle Laboratories Division, American Cyanamid Company, stating that Lederle was willing to sponsor a symposium. Four speakers from anywhere in the United States or Canada would be brought to Grand Forks to present this symposium. Dr. Harwood stated that he would desire the Third District Medical Society to agree to cosponsor this event along with the University of North Dakota School of Medicine. It was moved by Dr. Harwood, and seconded by Dr. Barcome that this be done. This was passed unanimously and a committee was to be named in the future to help select the speakers and the topics desired to be presented. A considerable amount of discussion was the next order of business regarding the mental retardation program which is being carried on, with Dr. Helenbolt presenting the views and desires of the mental health society of Grand Forks. Dr. Schafer then commented from the pediatrics viewpoint. Dr. Barcome urged that a committee of three be appointed by the president to look into this. We actively support the mental retardation program in this state and area. Dr. Helenbolt stated that he would leave the appointment of this committee up to the new president who takes office at the next meeting. A letter from John Alphso, States Attorney from Grand Forks County, was read in which he asked the Third District Medical Society to sponsor the sending of four peace officers to the U.S. Narcotics School. He stated that the cost of this would be approximately $600.00 per man. He recommended that four be sent, and that the pharmaceutical and medical society pay for two thirds of the cost of sending these men. There was considerable discussion concerning why the medical society and not the county or the city should pay for the cost of this. It was recommended by Dr. Mahowald and seconded by Dr. R. H. Leigh, that this matter be tabled temporarily, pending further discussion and investigation into this matter. This motion was passed. The Society then acted upon the application for membership of Dr. Lloyd Ralston, of Grand Forks. Dr. Ralston presented a transfer card from Bismarck, North Dakota. It was moved by Dr. Evans, and seconded by Dr. R. H. Leigh that the transfer be approved as presented, and this motion was passed unanimously. In the absence of Dr. Frank Hill, Chairman of the Nominating Committee, Dr. Prochaska presented the reports of the nominating committee regarding the appointment of officers for 1966. It was moved by Dr. James Leigh, and seconded by Dr. Barcome that the report of the nominating committee be considered as a whole, rather than voting on each office individually.

This was carried and the slate of officers presented by the nominating committee was as follows: President, R. C. Painter, M.D.; President-Elect, Harold I. Tarpley, M.D.; Vice-President, Curtis W. Sande, M.D.; Secretary-Treasurer, Thomas L. Schafer, M.D. Delegates to the State Medical Association were as follows: John A. Sandmeyer, M.D., G. L. Countryman, M.D., R. H. Leigh, M.D., Kenneth S. Helenbolt, M.D., Harold W. Evans, M.D., W. T. Powers, M.D. Alternate Delegates were as follows: Wallace W. Nelson, M.D., William P. Teevens, M.D., B. J. Clayburgh, M.D., Thomas L. Schafer, M.D., Norman M. Helgason, M.D., Richard K. Helm, M.D. Censor: John H. Graham, M.D. Blue Shield Board of Directors: Harold W. Evans, M.D.

Blue Shield Corporation: Wm. C. Nelson, M.D., R. C. Painter, M.D., R. Douglas Doss, M.D., John A. Sandmeyer, M.D., B. J. Clayburgh, M.D., Keith G. Vandergon, M.D., Robert H. DeLano, M.D., R. H. Leigh, M.D., George A. Wilson, M.D., William P. Teevens, M.D., Thomas J. Schafer, M.D., John H. Graham, M.D., and Frank A. Hill, M.D.

It was moved by Dr. Mahowald, and seconded by Dr. Clark that nominations cease, and a unanimous ballot was cast for the above officers. This motion was passed. Following the adjournment of the business meeting, the program was then turned over to Major Dees who presented two Air Force movies. The first one being on the SAC mission, and the second regarding the function of a medical unit in a disaster. Following these presentations, the meeting was adjourned.

The February meeting of the Third District Medical Society was held at the Bronze Boot Steak House. It was called to order by Dr. Robert Painter, the new President. Dr. Robert Elliott, Assistant Professor of Medicine, University of Minnesota Medical School, presented the following program. His paper was entitled "Unexpected Events During D.C. Cardio Version." This was followed by an interesting discussion of the problem as it related to the local area.

Dr. Joseph Craven, M.D., President of the North Dakota State Medical Association was introduced by Dr. Painter, and he presented his views on the problems as they face medicine at this time, and also what some of his feelings are concerning the solution of these problems. He strongly urged the support of AMPAC and COMPACT.

On a motion of Dr. Mahowald, and seconded by Dr. McLeod, the minutes of the January meeting were accepted without reading. The motion passed.

Committee appointments were made by Dr. Painter as follows: Program: W. C. Nelson, M.D., Chairman; R. K. Helm, M.D., and R. G. Clark, M.D. Awards: H. I. Tarpley, M.D. Legislative and Public Relations: B. J. Clayburgh, M.D., Chairman; W. T. Powers, M.D., W. W. Nelson, M.D., N. M. Helgason, M.D., W. P. Teevens, M.D., R. H. DeLano, M.D. Medical Review: R. C. Painter, M.D. Grievance Committee: H. I. Tarpley, M.D. Executive Committee: T. L. Schafer, M.D. Mental Health and Retardation: D. F. Barcome, M.D., Chairman; T. L. Schafer, M.D., K. S. Helenbolt, M.D. Hospitality: J. R. Olson, M.D. Liaison with the Valley Memorial Home, J. H. Graham, M.D. A communication was read from Dr. George Starcher, University of North Dakota, concerning our participation in the dietetic Intern Program that was to be instituted in the city. It was moved by Dr. Haunz and seconded by Dr. Evans that we endorse this program. The motion passed. The meeting was adjourned at 9:55 P.M.

Respectfully submitted,
(Signed) RALPH E. MAHOWALD, M.D.,
Councillor, Third District

Fourth District

The number of active paid-up members affiliated with this Society, as of April 1, 1966, is 50. There are 4 Honorary members. Six physicians were admitted during the last year to membership in the Society. They were:

A. J. FAULCONBRIDGE, M.D.	Mohall
D. HILIOPOULOUS, M.D.	Westhope
C. C. RAM, M.D.	Minot
VICTOR KALJOT, M.D.	Minot
PAUL VANDERSTEEN, M.D.	Minot
R. NATARAJAN, M.D.	Minot

The officers elected for the 1965-1966 year were:

President	GALE R. RICHARDSON, M.D.
Vice-President	G. M. HART, M.D.
Secretary-Treasurer	BRIAN E. BRIGGS, M.D.

From May 1965 through February 1966, the regular meetings of the Northwest District Medical Society were held on 6 occasions.

In May 1965 the delegates to the recently concluded North Dakota State Medical Association Meeting presented their report on the proceedings of that meeting. Dr. Edward O'Connell of the Department of Pediatric Allergy, The Mayo Clinic, then presented a paper on "Allergy in Children" dealing especially with bronchial asthma, milk allergies and dysgamma globulinemia.

No meetings were held in June, July, and August, 1965. In September 1965, Dr. Clifton Miller, Professor of Pharmacology, University of North Dakota, discussed "Uses and Abuses of Habit Forming Drugs," and then outlined the scope of public law 8974 in regulating the use of such drugs.

The speakers at the October meeting of the Society were J. D. Craven, M.D., President of the North Dakota State Medical Association and Willard Wright, M.D., Past Chairman of the AMA Council of Medical Services. These speakers discussed at length the impact of Federal legislation on the practice of medicine. Dr. Wright outlined the evolution of Federal involvement in the practice of medicine over the years and suggested that more was to be gained by responsible efforts by physicians through the AMA to modify and alter Federal legislative proposals to their advantage than by any general boycott.

In November 1965, Dr. Harold Katkov, Consultant in Pediatric Cardiology, University of Minnesota, presented a paper, with extremely interesting slides and cine-angiograms, on "Recent Advances in Pediatric Cardiology."

Dr. George Browning, U.S. Public Health Service, Aberdeen, South Dakota, spoke at the January 1966 meeting on "Comprehensive Medical Care for Indians." He stated that the aim of the U.S. Public Health Service was to raise the general health level of Indians to the highest possible level. The funds available to them were, however, limited, and they had of necessity to husband their resources and do the best they could under the circumstances. At this meeting, officers of the Society for the year 1966-67 were elected. They were:

President	W. C. HURLY, M.D.
Vice-President	L. A. GILTNER, M.D.
Secretary-Treasurer	B. JAYAPATHY, M.D.

In February 1966, delegates to the State Medical

Association and their alternates were elected. They were:

Delegates

L. A. GILTNER, M.D.; R. S. LARSON, M.D.; B. E. BRIGGS, M.D.; and A. M. CAMERON, M.D.

Alternates in the following order were:

Alternates

J. T. BOYLE, M.D.; S. E. SHEA, M.D.; W. B. HUNTLEY, M.D.; and S. W. KECK, M.D.

Dr. Kenneth Berge of the Department of Internal Medicine, Mayo Clinic, then presented a paper on "Hypercholesterolemia." He mentioned that current terminology was quite confusing and attempted a clarification of the various terms in use. He then dealt briefly with the various drugs that are used to reduce blood cholesterol—and with the importance of diet.

The Fourth District Medical Society has had an active year with excellent participation in its activities by its members.

Respectfully submitted,
(Signed) Frank D. Naegeli, M.D.,
Councillor, Fourth District

Fifth District

The Sheyenne Valley Medical Society held six dinner meetings during the fiscal year March 1965 through February 1966.

The first meeting was held on April 21, 1965. Dr. A. K. Saiki, Pathologist, University of North Dakota Medical School, held a pathological conference with a discussion of cases from this hospital, including presentation of slides.

The next meeting was held on May 19, 1965, with Rod Carlson, Fargo, North Dakota, discussing different types of investments of interest to doctors of medicine.

No summer meetings were held.

The first Fall meeting was held on September 15, 1965, with Dr. Robert Bushell of the Fargo Clinic, Fargo, North Dakota, discussing various obstetrical and gynecological problems.

On October 20, 1965, Mr. Don Eagles and Mr. Steven Pezalla presented the program, discussing the anticipated problems with Medicare, citing statistics as to hospital bed utilization by the affected group.

On November 17, 1965, Dr. James Hoyme, Psychiatrist at the State Hospital, Jamestown, North Dakota, spoke on the "Acute and Chronic Brain Syndrome."

The next meeting was held on January 19, 1966, with election of officers and delegates as follows:

President	M. O. BERG, M.D.
Vice-President	NEIL MACDONALD, M.D.
Secretary-Treasurer	JOHN W. GOVEN, M.D.
Delegate	W. R. JENSEN, M.D.
Alternate Delegate	C. J. KLEIN, M.D.
Blue Shield Corporation Members	G. CHRISTIANSON, M.D. and C. E. JENSEN, M.D.
Director of Blue Shield	C. J. KLEIN, M.D.
Program Chairman	W. R. JENSEN, M.D.

Following the business meeting, a movie was shown on "External Cardiac Massage."

Our next meeting was on February 16, 1966. Our speaker of the evening was Dr. Lester Shook, Radiologist, Fargo Clinic, Fargo, North Dakota, who spoke on "Radio Isotopes," as well as discussing X-ray diagnosis of various pulmonary and gastrointestinal lesions.

With the addition of D. J. Feist, M.D., Forman, North Dakota; W. A. Craychee, M.D., Oakes, North Dakota; and Gary Cody, M.D., LaMoure, North Dakota, the Fifth District now has a total active membership of ten.

Respectfully submitted,
(Signed) G. Christianson, M.D.,
Councillor, Fifth District

Sixth District

Attended Council Meeting May 2, 1965 at Grand Forks.

Appointed to State Task Force for Mental Health Planning, June 4, 1965. Attended State Task Force Meetings on June 25 (Jamestown), July 30 (Mandan), August 27 (Minot), September 24 (Fargo). Served on the Executive Committee which wrote the final report and specific recommendations. These were summarized and sent to the President of the State Medical Association.

Appointed to the Subcommittee for Children and Youth of the Bismarck Regional Mental Health Planning Committee, May 6, 1965. Attended numerous meetings and served on the Executive Committee.

Sixth District Meeting, May 19, 1965. Reports were given concerning the House of Delegates Meeting in Grand Forks. Special mention was made of the Medical Auxiliary's joint husband-wife billing. I gave a short report and asked that the District Society Treasurer also bill for AMPAC and COMPACT membership with the District Dues. Neither of these suggestions were acted upon favorably by the Society. Dr. Owens reported that 2,256 people had received tetanus shots in several clinics. It was decided to donate $200.00 to the Medical Auxiliary, $350.00 to the Boy Scouts and $350.00 to the Girl Scouts. The North Dakota Tuberculosis and Respiratory Disease Association offered $2,000.00 yearly for three years to establish a Pulmonary Diagnostic and Treatment Center at St. Alexius Hospital. The Society voted to accept this offer and establish the Center.

On May 22 and 23, 1965, I attended a National AMPAC workshop at the Shoreham Hotel, Washington, D.C. Addresses were given by Dr. Donovan F. Ward, Senator Everett M. Dirksen, Senator Spessard L. Holland, Rep. Wendell Wyatt, Rep. Joe R. Pool, Rep. Alton Lennon, Bryce N. Harlow and Rep. Paul Findley.

In September, 1965, Dr. Percy Owens announced his retirement from active practice. He will be employed by the State Health Department.

On September 11, 1965, I attended the Annual Regional Meeting of the American College of Physicians at Jamestown.

On September 29, the Sixth District Medical Society met with their wives and heard Mr. Oliver Field, Chief of the Investigative Division of the AMA, speak about Cancer Quackery. I gave a presentation concerning the Supplementary Medical Insurance Program of the Medicare Law. I stated that the National Association of Blue Shield Plans had been encouraged by the American Medical Association to assume an important role in the administration of the physician services portion of the Medicare Law (Part B). The Society voted to approve Blue Shield as a carrier for Part B.

Conference in my office with James W. Rosevear, AMPAC Field Representative, October 25, 1965.

Attended and moderated the Quain and Ramstad Clinical Conference, October 30, 1965.

Sixth District Meeting of November 17th was held under the direction of the Committee on Religion and Medicine. The Rev. Arthur Johnson of Fargo and Father Robert Benson of Jamestown, spoke and emphasized that theology is changing like medicine, and that the pastor should not be parochial but should approach his parishioners on a personal basis. During the business session the Society approved the involvement of the Medical Auxiliary in Community Mental Health and Retardation Center planning.

Conference November 24, 1965, with Mr. Fettig, Director of the Head Start Program for Bismarck. It was decided that the physical examinations would be done by the family physician who would bill the program his usual and customary charges.

Attended the Winter Council Meeting in Fargo, December 11, 1965.

On December 15, 1965, the following officers were elected by the Sixth District Society to serve during 1966.

President:	
PAUL KLOSTERMAN, M.D.	Bismarck
Vice-President:	
P. ROY GREGWARE, M.D.	Bismarck
Secretary-Treasurer:	
JOHN B. FRANKEL, M.D.	Bismarck
House of Delegates:	
PHILLIP DAHL, M.D., Term expires 1967	Bismarck
J. J. MOSES, M.D., Term expires 1968	Bismarck
M. A. K. LOMMEN, M.D., Term expires 1968	Bismarck
RALPH J. DUNNIGAN, M.D., Term expires 1968	Bismarck
C. J. BAUMGARTNER, M.D., Term expires 1966	Bismarck
EDMUND G. VINJE, M.D., Term expires 1966	Hazen
Alternate Delegates:	
ARTHUR EWERT, M.D.	Beulah
W. D. WALDSCHMIDT, M.D.	Bismarck
GRANDON TOLSTEDT, M.D.	Bismarck
W. J. ORCHARD, M.D.	Linton
P. R. GREGWARE, M.D.	Bismarck
Board of Censors:	
E. D. PERRIN, M.D., Term expires 1966	Bismarck
P. L. OWENS, M.D., Term expires 1967	Bismarck
R. W. HENDERSON, M.D., Term expires 1968	Bismarck
Board of Directors—North Dakota Physicians Service (Blue Shield)	
JOSEPH CLEARY, M.D., Term expires 1967	Bismarck
M. J. E. JOHNSON, M.D., Term expires 1967	Bismarck
EDMUND VINJE, M.D., Term expires 1968	Hazen
EDWIN BOERTH, M.D., Term expires 1966	Bismarck

The first meeting of 1966 was held on January 19th. Guest speaker, Guy Bevil, Director of Project Amigos De Las Americas, discussed the Project's program to provide medical aid to Latin America through young volunteers.

At the February 22nd Sixth District Meeting, we were addressed by Dr. Craven on the Medicare Law and the problems it will bring. During the business session, the Society discussed the Federal Regional Heart, Cancer and Stroke Program, area-wide hospital planning, and the Arthritis Clinic in Flasher. The Society voted to approve planning for a Regional Center.

During the year I have contributed more than 50 references to the Committee on the Medical Aspects of Driver Limitations. These were in the form of Thermofax copies.

I have established a file on Sports Injuries for Richard Karlgaard, Bismarck Schools Director of Athletics, and have contributed to this almost monthly.

The physician's prime moral obligation is to his patient, which includes nothing less than complete devotion, conscientious attention, and sustained diligence to the task of healing, together with rendering and procuring the best available medical care.

Respectfully submitted,
(Signed) R. B. Tudor, M.D.
Councillor, Sixth District

Seventh District

Since the last report, the following meetings were held of the Stutsman County District Medical Society. April 29, 1965. There was good attendance at this meeting with several guests. The principal guests were Dr. J. R. Amos of the North Dakota State Health Department, and Dean Harwood of the University Medical School. During the business meeting, Dr. Engberg, as President, appointed Drs. Hieb, Miles, Woodward, and Van der Linde, as a committee to represent the Medical Society for the Mental Health Program for the District. A resolution was passed, initiated by Dr. Swafford, to suggest to the forthcoming State Meeting that changes in the law should be made regarding liberalization of the abortion statute.

Dr. Harwood spoke on Current Trends in Medical Education, and named such highlights as the increasing number of four-year medical schools, the increase in the amount of federal money available for research programs, residencies, etc., and also that tuitions are becoming higher and higher. He pointed out that a large porportion of the medical students in this state were from lower income families than in any other state in the union.

Dr. Amos mentioned the numerous programs that the Public Health Department is carrying out; a total of forty-four such programs. The meeting was adjourned at 9:40 P.M.

The second meeting was held on October 28, 1965. At this meeting, the wives of the members were guests, and there were also guests from the State Hospital staff present. The principal event of the evening was a presentation by Lester Wold, M.D., of Fargo, reporting on his trip to the Honduras earlier in 1965 when he spent two months practicing medicine among the natives. This presentation was very interesting, and was very well received. The total attendance at this meeting was forty-eight.

The next meeting was held November 18, 1965. The guests at this meeting were Dr. Joseph Craven of Williston, State President; Lyle Limond, Executive Secretary; and Don Eagles and Steve Pezalla of the Blue Shield and Jim Rosevear for AMPAC. During this meeting there were three new members voted into membership; namely, Drs. Bernard March, Clinical Director of the State Hospital; O. P. Erickson, a staff physician at the State Hospital; and James Hockenberry of Oakes, North Dakota.

It was also moved and seconded at this meeting, and passed, that a committee be appointed to consider the fee structure at the local county level, and report back at the following meeting.

The program was presented by Dr. Craven of Williston who outlined the need for unity in the medical profession, and faith in the cause of organized medicine. Jim Rosevear, the AMPAC representative, made a request for dues for AMPAC. Mr. Don Eagles and Mr. Lyle Limond both commented on the Medical Economics Committee meeting regarding customary fee concept.

The next meeting was held January 20, 1966. Dr. Nierling presided at this meeting in the absence of the President and Vice-President. At this meeting there were three new members voted into the Society; namely, Dr. Fang L. Chiu, Dr. James B. Hoyme, and Dr. L. M. Cabanilla. All three of these doctors are members of the staff at the State Hospital here in Jamestown. At this meeting it was requested by the Auxiliary that a joint meeting be held at the regular February meeting. The Auxiliary requested this to increase their attendance at their meetings. The election of officers was held and the following officers were elected: Dr. Hubert A. Carbone, President; Dr. Philip Curtis, Vice-President; Dr.

Richard Nierling, Secretary-Treasurer; Dr. Edwin O. Hieb and Dr. James Miles were elected delegates to the annual meeting; Dr. Clement and Dr. Bishop were elected alternate delegates; and Drs. Elsworth, Curtis, and Woodward were elected censors; Drs. Sorkness and Clement were re-elected to be directors of the Blue Shield; and the following members were elected to the corporation of the Blue Shield, Drs. Sorkness, Clement, Miles, Van der Linde, Swenson, and Hieb.

The Secretary noted that the total dues for the year would be $200.00. The Secretary-Treasurer presented the financial report which was approved, and following this a film was shown produced by Merck Sharp & Dohme on the subject "The Management of Disabling Pain of Non-Arthritic-Rheumatic Origin." The final piece of business was the report of the committee which had been appointed for studying fees locally, and the report consisted of the fact that the fees had been established, that the California Relative Value Scale was being followed, and a five dollar conversion factor was used.

The next meeting was held February 17, 1966. At this meeting the wives of the members were present as guests. Mr. Ed. Sypnieski of the State Health Department spoke about the establishment of home care services under Medicare. Dr. Carbone, President, appointed Dr. Pederson as Program Chairman and suggested that he select one or two other doctors to aid him.

It was also decided at this time that there should be a change in our method of having business and scientific meetings and dinner; and it was decided that the business meeting would be first followed by the scientific meeting, and then later a social hour and dinner. Dr. Carbone's talk scheduled for this evening was postponed until the next meeting.

Respectfully submitted,
(Signed) John M. Van der Linde, M.D.,
Councillor, Seventh District

Eighth District

The local Kotana Medical Society held a dinner meeting on January 26, 1965 with election of officers for the coming year as follows: R. E. Wiederanders, President; M. J. Olson, Vice-President; Gyman Okeson, Secretary-Treasurer. The elected delegate to the State was Dr. Donald Skjei and alternate delegate, Dr. D. C. Oliver. There was a report given on Blue Shield affairs by Dr. Donald Skjei and the program consisted of current treatment covering endometriosis of the gastrointestinal tract presented by Dr. Robert Olson.

A dinner meeting on February 18, 1965 featured Dr. G. Alfred Dodds, President of the North Dakota State Medical Society, as the speaker. The wives were also entertained at this meeting.

On March 18 at a dinner meeting the program was presented by Dr. Eoin Harvey, who discussed the history and present development of the state of socialized medicine in Saskatchewan.

The District Society met again on April 8, 1965 when a dinner meeting was held with Mr. Glick, a member of the Treasury Department of the Bureau of Narcotics from Minneapolis, speaking to the group on the subject of narcotic addiction.

At a dinner meeting on May 20, 1965, Dr. Potts of the San Haven Sanatorium presented a program on the subject of nontuberculous chest diseases.

During October at a dinner meeting on the 5th, the members had a discussion on fees and Dr. J. D. Craven reported on the recent meeting of the House of Delegates from the AMA. The group was given an opportunity to hear Richard R. Reibert, Ph.D. of the Research Laboratory of Merck Sharp & Dohme speak on the advances in pharmacology and the drug industry. Mr. Andrew Hawkins, detail representative for the company, was also in attendance at this session.

New members taken into the District Society during the past year were Drs. Eoin Harvey, John Jamieson, and Robert C. Koch.

Respectfully submitted,
(Signed) Dean R. Strinden, M.D.,
Councillor, Eighth District

Ninth District

As of the date of this report, April 1, 1966, this District Medical Society has twenty-five active and four retired members and our activities for the year consisted of four meetings held throughout the year.

Our usual June meeting held in Mott was not held this year due to problems of scheduling.

Our first gathering was in October, 1965, when we spent a great deal of time going over reports of Blue Shield action as presented by Dr. Hankins and Dr. Gilsdorf, our two representatives on the Blue Shield Board of Directors. The scientific portion of the program consisted of a paper by H. L. Reichert, M.D. on "Serous Otitis" in children.

In January, 1966, we were honored by a visitation from Dr. J. D. Craven, President of the North Dakota Medical Association, who presented an interesting discussion on the upcoming Medicare Bill. At this meeting a new slate of officers was elected and they consist of Dr. Paul Ahlness, President; Dr. Donald Nicely, Vice-President; Dr. Richard Raasch, Secretary-Treasurer. Corporation Members: Drs. Ralph Dukart, Robert Hankins, Keith Foster, Amos Gilsdorf, and Walter Hanewald. Blue Shield Board of Directors: Drs. Gilsdorf and Hankins. Delegates to the State Medical Association: Drs. Walter Hanewald and Robert Hankins, with the alternate delegates being Drs. Robert Gilliland and Norman Ordahl. The Councillors of the District Society are Drs. Arnold Gumper, Donald Reichert, and Robert Thom.

In February, 1966, the meeting consisted of a presentation by Mr. Lester Ovre, Executive Director of the North Dakota Welfare Board, on points of mutual concern between the Welfare Board and local physicians. This was an excellent presentation and was very well received by the members of the Society.

Another informal meeting of the Southwestern District Society was held in March of this year when we met with the druggists in our Southwestern District area in an informal setting for a discussion of mutual problems that existed to both professions and an informal discussion on the recently passed Harris Act and its implementation. It was the feeling of the majority of people that we would institute a system in our area of the state where all prescriptions were only good for five refills or six months and after that became null and void.

Respectfully submitted.
(Signed) Keith G. Foster, M.D.,
Councillor, Ninth District

Tenth District

The Traill-Steele District Medical Society held four regular meetings during the past year. In the May meeting, 1965, Dr. Little, our Delegate, made an official report on the recent State meeting and on the important matters concerning the Society. A report was also given and a discussion held on Blue Shield and their recent changes and policies.

Our second meeting was well attended and our guest speaker, Dr. Robert Story, presented a talk on "Herald Angina" or Pre Coronary Disease."

The scientific speaker for our third meeting was Dr. D. T. Lindsay of the Orthopedic Department, St. Luke's Hospital, Fargo. He reviewed X-rays and treatments of problem fracture cases.

At our last meeting on February 9th, Dr. Patton of Cooperstown gave a discussion on the socialization of medicine in Great Britain.

During the past year Dr. Leckie of Cooperstown transferred out of State. Dr. Patton has entered practice with Dr. Kenneth Wakefield at Cooperstown.

At our February 9th meeting, the following were elected as officers:

President	DR. DONALD J. BREEN
Vice-President	DR. D. J. HLAVINKA
Secretary-Treasurer	DR. R. W. McLEAN
Delegate	DR. JAMES LITTLE
Alternate Delegate	DR. KENNETH WAKEFIELD
Council	DR. R. W. McLEAN
Corporate members—Blue Shield	DR. JAMES LITTLE and DR. R. W. McLEAN

Board of Directors—Blue Shield DR. D. J. BREEN (3 years), DR. KARL OJA (2 years) and DR. J. M. LITTLE (1 year)

Respectfully submitted,
(Signed) R. W. McLean, M.D.,
Councillor, Tenth District

STANDING COMMITTEES

Committee on Medical Education

No meeting of the Committee on Medical Education was held during the past year, therefore there is no report.

Respectfully submitted,
(Signed) Robert, J. Ulmer, M.D., *Chairman*
Committee on Medical Education
R. C. Painter, M.D., *Vice-Chairman*

Committee on Necrology and Medical History

Your lost friends are not dead,
but gone before,
Advanced a stage or two
upon the road
Which you must travel in the steps
they trod.
Aristophanes

JOSEPH ALFRED HILTS, M.D.

Dr. Joseph Hilts, 56, succumbed to a lingering illness at his home in New Salem on June 28, 1965.

He was born December 23, 1908 in Kennedy, Canada, and attended schools there and at Moosamin University, Winnipeg and the University of Saskatchewan at Saskatoon. His medical training was received at the University of Manitoba Medical School, Winnipeg, Manitoba, where he received his medical degree in 1939.

Following his medical education he practiced at Walpole, Canada, from 1939 to 1941; then at Whitewood, Canada, until moving to Bowbells, North Dakota in 1954. He then practiced in Hettinger from 1955 until moving to Mandan in 1960, where he maintained his practice until moving to New Salem in 1964. Dr. Hilts was a member of the Masonic Lodge, of which he was a Past Master, the Scottish Rite Bodies and the Shrine.

His first marriage was to Verne Lubienicki in Winnipeg in 1935. On June 9, 1961, he married Sharon Nelson at Glendive, Montana. She survives as do three sons and one daughter.

DANIEL W. MATTHAEI, M.D.

Dr. D. W. Matthaei, 82, a Fessenden resident for the past 50 years in the practice of medicine, passed away July 17, 1965 at his home there.

He was born December 4, 1882 in Labette County, Kansas, and graduated from high school in Kansas City and the College of Medicine of the University of Illinois in 1909. He interned at Poly Clinic, Chicago.

Dr. Matthaei began his medical practice in Arco, Idaho in the horse and buggy days of 1911 leaving there for post-graduate study in Chicago. He came to North Dakota and Fessenden on the opening day of the Wells County Free Fair in 1916. Following a year's practice in Fessenden he moved to Carrington where he became associated as a partner with Dr. O. W. McClusky. After a year and a half in Carrington, he bought a practice in Fessenden and occupied the same office until a few years ago when his health began failing. He had been Soo Line surgeon continuously since establishing his practice in North Dakota. He had served as Wells County Health Officer and on the Wells County Sanity Board for many years. Active in civic affairs, he had served as mayor and alderman of Fessenden, president and member of the school board and was active in the Civic and Commerce Association. He was a member of the Mystic Tie Lodge of Fessenden as well as Odd Fellow and Elks Lodge organizations. He held memberships in the American Medical Association, the North Dakota State Medical Association and the Tri-County Medical Society. He was awarded a Certificate of Distinction for 50 years in the practice of medicine by the North Dakota State Medical Association in 1963.

Dr. Matthaei was married to Hortense Day Fagin on December 19, 1920 at Carrington. She preceded him in death in 1955. He is survived by a daughter and two step-daughters.

FELIX F. VONNEGUT, M.D.

Dr. Felix Vonnegut, who had given continuous medical service to the Hague and Linton area residents for nearly half a century, passed away August 17, 1965 in a Bismarck hospital.

He was born February 2, 1895, at Jersey City, New Jersey, and attended public school there until 1905. After that his education was completed in Germany where his family moved to operate a branch of a business established in the United States. Privately tutored for a time, he attended the Oberrealschule in Muenster, graduating in 1914. During 1914-16 he studied medicine in Muenster University, then studied in Bonn University for two years. From 1917 until 1919, he was a student of medicine in the University of Rostock, Mecklenburg, from which institution he received his M.D. in 1919.

He served as an intern in several hospitals and remained in Germany doing clinical work until 1922. After his return to America, Dr. Vonnegut spent several months in Winnipeg, and then located at Hague in 1922 and remained in that community for over 21 years, moving to Linton in October, 1943. In 1926 he became Health Officer for Emmons County and held that position up to the time of his death. He kept a record of all deliveries he had supervised and by 1965, the figure had reached 4,725.

Dr. Vonnegut married Heldegard Franke at Rostock, Germany, August 11, 1920. She survives him as do two daughters.

OLAF J. HAGEN, M.D.

Dr. Olaf Hagen, 93, celebrated educator and physician, passed away December 3, 1965, at the Fargo Nursing Home, where he had been a resident for three years.

He was born September 16, 1872 at Menomonie, Wisconsin and in 1873 came with his family to a farm near old Fort Abercrombie. There he grew to manhood, working on farms and teaching school. At the age of 19 he became an instructor in history at Concordia College in Moorhead. At 23 he became superintendent of schools in Richland County, North Dakota and it was in that position that Dr. Hagen established the first consolidated school west of Illinois. He was asked to serve as superintendent of public instruction of North Dakota but declined having decided to enter the field of medicine.

He attended St. Cloud State College, the University of North Dakota, and later graduated from the University of Minnesota Medical School in 1906. He was licensed in North Dakota in 1907 and was a founder and first president of the Fargo Clinic, and had been a member of the surgical staff at St. Luke's Hospital for 30 years.

Area residents who followed the career of Dr. Hagen were constantly amazed at his activities, even in later years. Always interested in education, he served Moorhead as a member of its school board, was president of the Clay-Becker County Tuberculosis Sanitorium Board; President of the Northern Minnesota Medical Association, councilor for Minnesota of the American College of Surgeons; succeeded the late Dr. Charles Mayo as president of the Minnesota Public Health Association; member of the State Board of Health; member of the State Teachers College Board, and was elected by the State Legislature in 1931 as a member of the board of regents. In 1936 he was elected president of the National Governing Boards of State Universities and Allied Institutions in 31 states and in 1937 was elected to the executive board of that organization. In 1950 he started writing an historical account of the Red River Valley's early days. He was then 78 years old and while working on the book he continued to keep regular office hours as a doctor. Dr. Hagen had been so recognized nationally that his biographical sketch appears in "Who's Who in America" and also in "International Encyclopedia of World Biography."

Dr. Hagen married Moselle Edna Weld, daughter of Dr. Frank Weld, who had been president of MSC for 20 years. She preceded him in death. He is survived by a daughter and a son.

GEORGE U. IVERS, M.D.

Dr. George Ivers, 59, Cass County Health Officer and practicing Fargo physician, collapsed in Cass County Court, January 26, 1966, and was dead on arrival at a local hospital.

Dr. Ivers was born at Abercrombie, North Dakota, April 7, 1906. He received his early education there and at Concordia Academy; his B.A. degree at Concordia College; his B.S.M. degree from the University of North Dakota; and his M.D. degree from Rush Medical College in Chicago. He interned at St. John's Hospital in Fargo and in Los Angeles, California, after which he returned to Fargo practice. He had interrupted his studies to teach school in South Dakota for one year.

He had, for some time, been associated with the Veterans Administration and with the Northern Pacific Railway. His interests included many hobbies, with the collection of antique items being of special interest. He was associated with the museum at Abercrombie, North Dakota and was president of Cass County Historical Society. Dr. Ivers was a member of the Fargo Elks, Fargo Homecraft Club, the Moorhead Stamp Club, a member of the Masons, El Zagal Shrine and Scottish Rite Bodies, Veterans of Foreign Wars and of the Reserve Officers Club.

Dr. Ivers married Alice Myhre, April 8, 1953 in Fargo, and he is survived by her.

Respectfully submitted,
(Signed) E. H. Boerth, M.D., *Chairman*
Committee on Necrology and
Medical History

Committee on Legislation

This Committee has not been very active this year. In instances where it may have been active, it has been primarily through the function of the individual members of this committee in contacting the Federal Government representatives regarding Medicare which was in the offing at that time.

Your Chairman did contact our representation in Washington and received an exceedingly good reply from both Milton Young and Mark Andrews. The report which I received from Roland Redlin was not particularly significant except he did indicate that he would look into the situation before he cast his vote. As far as Burdick was concerned, he definitely took a stand that the Social Security approach to the practice of medicine for individuals past the age of 65 was the only method of approach in view of the fact that medicine in general had not made any attempt to correct a situation which existed and many people were apparently without care. This could be debated pro and con. There is little need for me to go into the medical viewpoint of this, because I feel that most medical men would agree with me that few, if any, people in this immediate jurisdiction have suffered because of medical neglect.

The thing that is now before us is a new legislative session which is coming up in 1967. It would appear that the State office should get on the ball to some extent to see that our State is properly divided into legislative districts medically and pick key men in the medical district, such as we have done in the past, and preferably men who are acquainted with the representation from such districts. There is little question in my mind that there will be some turnover at the coming elections insofar as representation is concerned, but it also appears to me that it might be well to get rolling on this prior to the November election. Any changes that may come in, thereafter, would be contacted after the election. The personnel that might come in should be checked as to whom they doctor with, in what district, and then approach them through their individual doctors.

Essentially speaking, I have very little to offer at this time except to indicate that I do not feel that the Medicare program as it exists at the present time is the ultimate approach that the Federal Government intends to take. It is my impression that they will undoubtedly recommend that the benefits of Medicare be expanded. As I view this thing at the present time, it appears that we may become totally socialized eventually even if it is not now.

I would indicate at this time that I am not totally satisfied with the representation that the AMA has made insofar as the rest of the divisions are concerned. I have expressed this to the AMA and have been assured that the "powers that be" will represent all individuals in this country equally. I must still express my view that I feel this is not so. It has come to the point where the AMA is so potent and powerful in many respects that the individual has very little, if anything, to say about what constitutes his will. This in effect, as far as I am concerned, constitutes one of the strongest unions that we have in the country.

This constitutes what I have to say. There is little question but what there will be many who will disagree with this statement. Should there be, it is a very small matter to change the Chairman and Committee.

Respectfully submitted,
(Signed) O. W. Johnson, M.D., *Chairman*
W. M. Buckingham, M.D.,
Vice-Chairman
Committee on Legislation

Committee on Public Health

A portion of this Committee met in Fargo, North Dakota, on Sunday, December 12, 1965, at the Gardner Hotel. The meeting commenced at 10:15 A.M. This was essentially a meeting of the Advisory Committee of the North Dakota State Medical Association to the Safety Responsibility Division of the State Highway Department. Members present were: R. W. McLean, M.D., Chairman; R. R. Ivers, M.D.; G. M. Hart, M.D.

Others present were: K. J. Kucera, Safety Responsibility Division of the North Dakota State Highway Department; J. R. Amos, M.D., North Dakota State Health Officer; P. L. Owens, M.D., Chairman, Committee on Public Health; J. D. Craven, M.D., President, North Dakota State Medical Association; J. Sherwood Williams, Field Services Division, AMA, and Lyle A. Limond.

This was the first meeting of this medical advisory committee which was appointed by the President of the North Dakota State Medical Society. Among other things, consideration was given by the members as to the feasibility of making revisions on the present use asking the applicant for more specific medical information.

Dr. McLean asked the cooperation of doctors throughout the State with the Highway Department. Mr. Kucera asked for permission to send material to the members for review such as one particular case involving driving disability for their consideration.

A motion was made by Dr. Ivers that any drivers renewal case involving medical factors be forwarded by the Highway Department to all members of the committee for their individual consideration. They should then be sent to the Chairman of the Committee for his evaluation.

This final opinion is then to be directed to the office of Mr. Kucera.

Meeting was adjourned at 12:30 P.M.

Respectfully submitted,
(Signed) Percy L. Owens, M.D., *Chairman*
Committee on Public Health

Committee on Public Relations

There has been no meeting of this Committee since the undersigned became its Chairman.

Mr. Daniel Buchanan resigned his position as Director of Public Information and Education and so far, has not been replaced. The post, by action of the Council, is now to be known as "Office of Assistant Executive Secretary and the Director of Public Information and Education."

Public Relations, like charity, begin at home—you can't buy them, you have to make them.

Respectfully submitted,
(Signed) W. M. Buckingham, M.D., *Chairman*
F. A. DeCesare, M.D.,
Vice-Chairman
Committee on Public Relations

Committee on Official Publication

There was no meeting of the Committee on Official Publication during the past year.

Respectfully submitted,
(Signed) Joseph W. Cleary, M.D., Chairman
Committee on Official Publication

Committee on Medical Economics

The Medical Economics Committee has met on three occasions since the last report.

The first meeting was not held until November 13, 1965, hoping for more information on P.L. 89-97 which was signed by President Johnson on July 30, 1965, and because of attendance at the National Orientation Conference on P.L. 89-97 in Chicago on October 1, 1965.

At our first meeting on November 13, 1965, Mr. Lester O. Ovre, Executive Director of the Public Welfare Board, presented information on the Medical Assistance Program, Title XIX of P.L. 89-97. He informed the committee that the Public Welfare Board of North Dakota would start this new program on January 1, 1966. He also stated that Title XIX might also deal with a group known as "medically needy" children. He requested a realistic fee in the Relative Value Schedule for mileage in rural areas.

At this same meeting the following were accomplished:

1. It was moved and passed unanimously that "The Medical Economics Committee of the North Dakota State Medical Association subscribes to the principle of usual and customary fees as a basis of fees charged."
2. It was moved and passed unanimously that "All charges billed the Public Welfare Board of North Dakota be the usual and customary fees charged any person."
3. It was moved and passed unanimously that "Mileage in rural areas be at 0.2 units per mile, one-way, from city limits to the patient."
4. A request from O.D.M.C. to reduce fees on six different procedures was denied by the committee.
5. A three-man subcommittee was appointed to deal with matters pertaining to O.D.M.C.

On November 22, 1965, Mr. Leslie O. Ovre was informed by letter of motions number 2 and 3 above. On November 18, 1965, Brigadier General Norman E. Peatfield of O.D.M.C. was informed by letter of the committee's action on the request for reduction of fees and also of the committee's subscribing to the principle of usual and customary fees.

The second meeting of the Medical Economics Committee was on December 10, 1965. The committee heard Mr. George W. Wells of the Health Insurance Council, Chicago, Illinois, give a plea for the private insurance companies in any endorsement of a carrier for Part-B, Title XVIII of P.L. 89-97. Dr. W. B. Huntley, Chairman of the Rates and Underwriting Committee of Blue Shield, spoke on a Blue Shield study of the proposed use of usual and customary fees and its effect on premiums. He read a resolution passed unanimously by the Blue Shield board supporting the usual and customary fees as recommended by the Medical Economics Committee, but asking for 25% reduction for medical services to those in the low income group (under $6,000.00 per year income).

Reports were then given by various committee members assigned to certain sections of the Relative Value Schedule in planning the revision of this schedule. Specialty societies had previously been written for their suggestions. In addition to committee member reports, the committee also heard special reports from Dr.

Donald Lamb on plastic surgery, Dr. John Rawland on anesthesiology and Dr. Lee Christoferson on neurosurgery. Mr. Howard Brower of the State Medical Society of Wisconsin then discussed P.L. 89-97 with a question and answer period following his presentation.

The following motions regarding possible conversion factors for various third parties were made and passed unanimously.

1. "The figures we give the Public Welfare Board for negotiation, based on the 1958 schedule and the 1962 revision, plus the 1964 California Schedule, be: Medical, 4.50; Surgery, 4.50; X-ray, 5.00; Laboratory, 5.00."

2. "That the same motion apply to all federal agencies."

The third meeting of the Medical Economics Committee was held on March 19, 1966. Mr. Donald Eagles, Executive Vice-President of the Blue Shield, explained some of the tentative guide-lines laid down for carriers administering Part-B, Title XVIII of P.L. 89-97. These guide lines centered around the obtaining and organizing data on customary charges made by physicians and the necessary close working relationships of the carrier with the medical societies in its geographical area to deal with matters related to determination of reasonable charges, etc. Blue Shield is now making a confidential survey of 1966 usual and customary fees being charged by members of the North Dakota State Medical Association. The Medical Economics Committee endorsed this survey unanimously and a letter to this effect will be sent to members of the North Dakota State Medical Association.

The Committee then heard comments from Dr. Percy L. Owens, Director, Health Insurance Division, State Department of Health, on Part-A, Title XVIII, P.L. 89-97, regarding certification of hospitals, private laboratories, extended care facilities and home health agencies.

A letter from Mr. Leslie O. Ovre, Executive Director, Public Welfare Board of North Dakota, dated March 1, 1966, was read. The letter reads as follows:

> "The Public Welfare Board expects to adopt the same system of making payment through the Medical Assistance Program, Title XIX, as is adopted in making payment through the Health Insurance and Medical Care for the Aged Program, Title XVIII. The Public Welfare Board, however, cannot divest itself of the responsibility of determining if the charges made by any medical vendor are 'reasonable.' In this respect the Public Welfare Board does not expect to have any difficulty with the North Dakota Medical Association or any of its members."

The proposed letter to be sent to various State and Federal agencies regarding the use of usual and customary fees was approved by the committee. This will take effect with all agencies at the end of their 1966 fiscal year.

R. W. Henderson, M.D., Medical Consultant, Public Welfare Board, discussed the need for additional items to be included in the North Dakota Relative Value Schedule, along with a relative value. It was pointed out that the majority of the suggested additions can be found in the 1964 California Relative Value Study. Such additions and revisions will be included in the proposed revision of the North Dakota Relative Value Schedule.

A group of anesthesiologists appeared before the committee to further expand the presentation that had been made at the December 10, 1965 meeting of this committee. They suggested that anesthesia values be based on time units only and not a basic value plus time units.

A letter from three practitioners regarding certain skin testing procedures for allergies was referred to the claims review committee of Blue Shield.

Our Executive Secretary had received a letter from Wallace Pianka, M.D., Chief Medical Officer of the V.A. office in Fargo regarding the Veterans Administration's recommended fee schedule. This fee schedule follows the 1964 California Relative Value Study, more or less. The letter and proposed fee schedule were discussed. The committee felt that the letter to be sent to various State and Federal agencies regarding the use of usual and customary fees would take care of this problem.

Since all the necessary data from Specialty Societies was not as yet received, the committee postponed further work on the revision of the Relative Value Schedule until the next meeting of the committee.

A grievance committee will be appointed from members of the Medical Economics Committee to deal with the carrier (Blue Shield) for Part-B, Title XVIII, P.L. 89-97, on problems related to reasonable charges.

Your chairman and Mr. Lyle Limond attended the National Conference on Federal Medical Assistance Programs in Chicago on January 20-21, 1966.

Future work of the Medical Economics Committee will consist of:

1. Completing the revision of the Relative Value Schedule.

2. Dealing with third parties on any problems arising from the use of usual and customary fees by members of the North Dakota State Medical Association. The revised Relative Value Schedule will be used as a "guide" in relating one procedure to another and thus aid in the determination of reasonableness of a fee. Generally speaking, conversion factors will not be negotiated.

3. Conferring with the Carrier (Blue Shield) for Part-B, Title XVIII, P.L. 89-97, through the committee's subcommittee (grievance committee) on problems related to reasonable fees.

4. Cooperating with Blue Shield on development of service plans.

It is recommended that when a new Medical Economics Committee is appointed by the President of the North Dakota State Medical Association, that other specialties be included in its membership so that all specialties will be represented on the committee. Besides the specialists already on the committee, it is suggested that the following specialties be represented: 1) anesthesiology, 2) plastic surgery, 3) psychiatry, 4) pediatrics, 5) neurosurgery, 6) urology.

Respectfully submitted,
(Signed) O. V. Lindelow, M.D., *Chairman*
J. F. Houghton, *M.D., Vice-Chairman*
Committee on Medical Economics

SPECIAL COMMITTEES

Committee on Cancer

The Cancer Committee of the North Dakota State Medical Association had two formal meetings during the past year, one of which was held in conjunction with the State Meeting at Grand Forks in May 1965 and the second meeting December 10th at Fargo where the Interim Meeting of the Council was held. These meetings eventually became informal in nature and at times were on a catch-as-can basis as the agendas at both meetings were crowded with the more important problems of medical legislation and medical economics which deserved precedence over routine committee sessions. However, we were able to discuss projects for 1965-66, which filtered down to two categories.

It was felt that more emphasis should be called to the attention of our colleagues regarding the important place of Cancer Control in Pediatrics. Statistics reveal that between the ages of 3 and 15 the most common cause of death is accidents. The next common cause of death is Cancer. In 1957 the North Dakota State Cancer Society had a team of two doctors from the Mayo Clinic on the Cancer Caravan discussing this subject in hopes of stimulating more attention to this important specialty in relation to Cancer. We have contacted the Executive Director of the State Cancer Society who, in turn, will cooperate with us in obtaining pediatric literature which will be sent to the medical profession in the State. Perusal of this subject will depend on the reception this receives.

Dr. Warren Cole, a former president of the American Cancer Society and head of the Department of Surgery at the University of Illinois, informed us that soon there will be available a new film on "Diagnosis and Treatment of Cancer of the Colon." We are patiently awaiting the arrival of this film and would like to book a viewing with each of the District Medical Societies. Emphasis is placed on the use of the Procto-sigmoidoscope as a diagnostic tool. Statistics reveal that incidence of Cancer of the colon is higher than other areas of the G.I. tract.

We note in National Medical, Surgical and Cancer Journals that more emphasis is being placed on 6 areas of the body which have the highest incidence of cancer; namely, the Skin, Breast, Lung, Stomach, Uterus and Cervix and Colon. With this in mind, your committee will direct our efforts to cancer education and cancer control.

During the past year, Mrs. Mary Snyder, founder and Executive Director of the North Dakota Division of the American Cancer Society, retired from active duty, pioneering a long, arduous struggle to place Cancer Control to the highest level to which it rightly belongs before the doctors and public of North Dakota. I am sure that very few realize the numerous road blocks and discouraging events that one meets in directing and guiding such a program. Having experienced the ravages of cancer in her own family served as a stimulant to her undaunted courage to help save lives of others who needlessly and previously had become victims of cancer. In her retirement, Mary can be rightly proud of her achievements. All of us are proud of her, too. As I reflect and scan her years of cancer activity, I wonder how many lives she has saved? Probably more than any doctor.

Dr. John Elsworth of Jamestown is top man of the North Dakota Cancer Society, taking over the position of President for 1965-66. His predecessor, Dr. O. W. Johnson, has left this position a tough spot to fill, but I am sure that John is fired up to the need of this organization in the State. He is well qualified and will make an excellent President. Dr. John Gillam continues as Chairman of the Executive Committee. We urge you to give your help, support and guidance to the county commanders in your vicinity. If any of you wish any cancer pamphlets or material along this line, do not hesitate to write to us, or write to Mel VanBeek, our Executive Director, Box 426, Fargo, North Dakota.

Respectfully submitted,
(Signed) Carroll M. Lund, M.D. *Chairman*
Committee on Cancer

Committee on Nursing Education

Your Committee on Nursing Education had no formal meeting of itself; however, met in conjunction with the Committee on Professional Nursing Practice from the State Nurses Association on January 20, 1966. M.D.'s present were Dr. Alice Peterson and Dr. T. H. Harwood. You have previously been briefed on the joint statement concerning intravenous therapy. The Medical Association approved the total joint statement previously agreed upon with the exception of Item 4-C, which item gave the physician the major weight in the decision made working towards standard operating procedures. Guiding principles for the administration of anesthetics were set up at this meeting including the following requirements:

1. A general anesthetic should be given by a qualified person. A qualified person is defined as a physician or nurse anesthetist who has completed an approved course of training in anesthesia.

2. The patient should not have eaten within the past few hours. A general anesthetic should not be used unless it can be presumed that the patient's stomach is empty.

3. The anesthetist should be in constant personal attendance throughout the entire procedure and assist in the patient's care until taken to his or her room or the recovery room.

Objectives:

1. Help to promote improved patient care. No patient receiving a general anesthetic should be denied the basic minimal essentials for a safe general anesthetic.

2. Promote education of the nurse anesthetist and give greater recognition to the nurse anesthetists in North Dakota. No anesthetic should be given by a person who has not successfully completed an approved course in anesthesia.

3. Increase the number of nurse anesthetists in North Dakota. The recognition of the need to increase the number of nurse anesthetists in North Dakota: A. Because of lack of qualified nurse anesthetists available. B. Importance of role played by the nurse anesthetist. C. Take positive steps to insure the availablity of nurse anesthetists in North Dakota by: (1) Student aid programs. (2) Promotion of schools of anesthesia in North Dakota.

Respectfully submitted,
(Signed) Glenn W. Toomey, M.D., *Chairman*
Committe on Nursing Education

Committee on Maternal and Child Welfare

The Maternal and Child Welfare Committee had to meet by telephone because of the blizzard, and the following recommendations have been made by the Committee:

1. Tests of Infants for Inborn Metabolic Errors Causing Mental Retardation. It is the duty of the administrative officer or other person in charge of each institution caring for infants 28 days or less of age and the person required in pursuance of the provisions of Section 23-02-12 North Dakota Century Code to register the birth of a child, to cause to have administered to every such infant or child in its or his care, tests for phenylketonuria and other inborn errors of metabolism causing mental retardation in accordance with rules or regulations prescribed by the State Department of Health. Testing and the recording and reporting of the results of such tests shall be performed at such times and in such manner as may be prescribed by the State Department of Health.

2. A vaginal examination is a sterile procedure. This procedure is done with a sterile glove and pHisoHex, liquid soap to guard against infection. A sterile glove and pHisoHex is required each time procedure is executed.

With the objective of protecting the patient, the doctor, the professional nurse and the hospital, the North Dakota State Medical Association, the North Dakota Hospital Association and the North Dakota Nurses Association acknowledge their acceptance of the legal right of licensed professional nurses to perform this procedure, with the exception of the following conditions: 1) preceding active or early mature labor; 2) or refusal by the patient, and if the following conditions exist:

A. The nurse has had special instructions in the procedure and her competency verified.
B. The nurse performed the vaginal examination upon the order of a licensed obstetrician for a specific patient.
C. In a hospital or any health agency, the procedure is to be performed within the framework of designated preparation and practice established for the hospital or agency by a committee composed of representatives from the Obstetrical Staff, Medical Staff, the Department of Nursing and the Administration. This framework of preparation and practice is to be reproduced in writing and made available to the total Medical, Obstetrical Staff and Nursing Staffs.
D. It is the jurisdiction of that Committee in a hospital or organized agency to: (1) Determine which nurses in the O.B. Department may perform vaginal examinations. (2) Establish in-service training of the procedure for all licensed professional nurses needing this instruction. (3) We had been asked to study the following recommendation:

Now, therefore, be it resolved that the North Dakota State Medical Association recommend that Section 12-25-01 be amended, by adding the following:

A licensed physician is justified in terminating a pregnancy if:

A. He believes that there is substantial risk that continuance of the pregnancy would gravely impair the physical or mental health of the mother or that the child would be born with some grave physical or mental defect, or the pregnancy resulted from rape, or from incest; and
B. Two physicians, one of whom may be the person performing the abortion, have certified in writing their belief in the justifying circumstances, and have filed such certificates prior to the abortion in the licensed hospital where it was to be performed, or in such other place as may be designated by law.

The Committee felt that this should be revised in some parts and made more specific and then more study be given before any definite recommendations can be made.

Respectfully submitted,
(Signed) Robert E. Lucy, M.D., *Chairman*
Committee on Maternal and Child Welfare

Committee on Foreign Trained Physicians

The large scale migration of foreign educated physicians to the United States is relatively recent. It is the largest international migration for post-graduate education in any field in history.

There is a tremendous world-wide deficit of physicians, and this deficit is now apparent in the United States, where more medical schools are essential and those now in operation should consider increasing the number of their graduates. Prior to 1950, the number of foreign medical graduates entering the United States was so small that no accurate count was kept, but currently more than 24% of the residents in the United States are foreign trained.

The foreign medical graduate is a problem for State Licensing Boards and for hospitals who seek their services as interns and residents. This problem has been somewhat facilitated by the creation of the Educational Council for Foreign Medical Graduates (E.C.F.M.G.), which began operations in 1957. The agencies sponsoring the E.C.F.M.G. are the AMA, Federation of State Medical Boards of the United States, the Association of American Medical Colleges, and the American Hospital Association. Since 1961, all interns and residents from abroad are required to pass the E.C.F.M.G. examinations, and this screening test has been of great value in evaluating the medical knowledge of each candidate.

The educational exchange act of 1948 was designed to bring foreign trained physicians to the United States, place them in approved training centers for a period of three years, following which time they would return to their native land and apply the knowledge and skill developed in the United States to improve medical care in their homeland. This plan was highly idealistic and actually never did fulfill its intent for at least two reasons. First, many of these physicians remained permanently in the United States by having their visas extended, by utilizing changes in the immigration act, and by marrying American girls. Secondly, it is now realized the program was impractical as their surroundings at home lacked the equipment and personnel under which they had been trained and had had access to in the United States.

As time passed, they did function to pick up the slack between the number of approved internships and residencies in the United States, 12,000 plus and 10,000 plus, and the number of physicians graduated each year by our 85 medical schools, 7,000 to 8,000.

In additon, our many state hospitals for the mentally ill and the tubercular found need of the services of foreign graduates (75% employed in the state hospitals in the United States are foreign trained), and the smaller communities eager for a physician welcomed them as soon as they could obtain a medical license.

The language difficulty remains a serious problem. To overcome this, many hospitals have instituted courses in English and in social development. Hospitals which employ all foreign trained graduates, both as interns and residents, are especially in trouble as the staff then loses interest in teaching and a sub-standard service results. This is unfortunate for both the residents and the hospital. These defects cannot be corrected in a few days. It is now recognized that the hospitals affiliated with medical schools should try to include a few foreign graduates on their house staffs. It is very necessary to assure that foreign trained physicians, whether here on temporary or permanent visas, do not have an unfavorable impact on existing high standards of medical care in the United States. While many organizations in the United States are helpful in the selection, guidance, training, and placement of certain categories of foreign physicians, it is unfortunate that the vast majorities of foreign physicians in the United States today did not have these services available. This constituted the greatest detriment to the fulfillment of the intent of the Education Exchange Program.

Data: 1965:

Foreign Graduates in the United States as interns	2,821
Foreign Graduates in the United States as residents	8,140
Other Graduate Trainees	1,925
Total	12,886

(Canadian Graduates are not considered foreign)

Non-citizens who are graduates of United States Medical Schools, 235.

About 80% of the foreign interns and 70% of the foreign residents in the United States come from developing countries (Asia, Africa, Latin America, and the Middle East), who actually have no physicians to export. The Philippines, Iran, Turkey, and Korea are especially represented.

In the period 1958-1964, 87,148 Foreign Graduates were examined by the E.C.F.M.G. 60% eventually passed after one or more trials.

States not accepting Foreign Graduates for licensure are, Arkansas, Louisiana, Nevada, and Oklahoma. Neither does Puerto Rico. All states except eight require an E.C.F.M.G. Certificate for licensure. Twenty states will license foreign graduates by either reciprocity or by endorsement of some other state.

Since 1930, 47,734 Foreign Graduates have been examined by State Licensing Boards in the United States, with a failure rate of 40.9%.

In 1964, 1,031 Foreign Graduates wrote the examination for licensure in 47 states. Failure rate, 32%. U.S. Graduates failure rate, 1.7%.

Foreign Graduates licensed in the United States since 1950, 15,462.

Relative to North Dakota:

Forty-seven Foreign Graduates are now licensed in North Dakota; 25 in a specialty and 22 in general practice.

For the period of time 1960-1965, 37 Foreign Graduates were examined in North Dakota. 29 were licensed and 8 failed.

In 1965, 7 Foreign Graduates wrote the North Dakota State Board examinations; 1 failed.

Respectfully submitted,
(Signed) C. J. GLASPEL, M.D., *Chairman*
Committee on Foreign
Trained Physicians

Committee on Diabetes

Members of Committee: Drs. E. A. Haunz, Chairman, Grand Forks; D. M. Barnard, Fargo; B. Hordinsky, Drake; W. R. Jensen, Valley City; E. O. Hieb, Jamestown; W. H. Wall, Wahpeton; D. G. McIntyre, Rugby; G. H. Heidorn, Minot; K. G. Foster, Dickinson; P. F. Klosterman, Bismarck.

The Committee on Diabetes, initiated by Dr. Leonard Larson of Bismarck, has continued its primary function to encourage and coordinate annual diabetes detection drives throughout the state under sponsorship of constituent local medical societies. This function is a cooperative effort in support of National Diabetes Week, sponsored in November each year by the Committee on Detection and Education of the American Diabetes Association, Inc. Increasing participation is in evidence among district medical societies throughout the nation. Last year, well over one thousand societies held individual detection drives.

Unfortunately, during 1965 there was virtually no activity in diabetes detection through the state of North Dakota.

The State Health Department has repeatedly voiced its interest in participating in diabetes detection in cooperation with the North Dakota State Medical Association and interested physicians throughout the state. It is hoped that in the future a joint cooperative effort may be made with the State Health Department to carry out diabetes detection programs on a larger scale and more efficiently in the future. However, the committee feels that it is most important that the medical profession throughout the state try to maintain the initiative and leadership in this overall project. In fact, diabetes detection drives throughout the United States have been almost exclusively carried out under the sponsorship of local medical societies. This not only stimulates more enthusiasm among participating physicians but sustains the good will which has been engendered toward the medical profession in carrying out this free service to the public throughout the past decade.

This committee sincerely hopes that constituent medical societies of the North Dakota State Medical Association will give serious thought to carrying out some sort of diabetes detection program in 1966. The expense involved in these drives is minimal because of the cooperative effort of various pharmaceutical manufacturers in furnishing free testing material and the American Diabetes Association, Inc., is glad to cooperate in furnishing publicity materials to assure a uniformly ethical approach throughout the different projects.

I would again like to express my appreciation for the continued excellent cooperation from committee members throughout the year who stand ready to cooperate at any time detection programs are initiated by individupal groups.

Respectfully submitted,
(Signed) E. A. HAUNZ, M.D., *Chairman*
Committee on Diabetes

Committee on Crippled Children

The Committee on Crippled Children held a business meeting Saturday, December 11, 1965, at the Gardner Hotel, Fargo, North Dakota. The meeting commenced at 9:55 A.M.; Dr. Paul L. Johnson, Chairman, presided.

Present were Drs. Ralph Vinje, B. A. Mazur, J. V. Miles, D. T. Lindsay, G. M. Hart, A. E. Culmer, Jr. Also present was Myrtle Kohler, Recording Secretary.

The Chairman, in his opening remarks, advised the members that during the past year he had served at various times in place of Dr. Paul W. Freise, Medical Director of the Crippled Children's Services, during his temporary absences from the Public Welfare Department. He added that in view of the fact that all costs had risen, that an increase in rates should have been requested. It was pointed out that orthopedic diseases had decreased to approximately 1/3 to 1/2 of the total case load, whereas when it was originally established that the program was mainly that of orthopedic entities. The Chairman further felt, in his opinion, that the Welfare Board should continue to screen cases for medical and financial acceptance very carefully and that all approvals should continue to be signed by the Welfare Director as a further check on financial eligibility. At the county level, there should continue to be very careful evaluation of cases. There was an approximate 10% increase in the total number of cases approved during the fiscal year 1965 and it was felt that this could be attributed to increased efforts on the part of county welfare personnel. Finally, it was felt that continued careful screening at the state level should be performed in order to exercise continued careful control at the county level.

It was also pointed out in a report to the Medical Economics Committee by Mr. Ovre that possible extension of Crippled Children's Services was considered in which all medically indigent children would be accepted to the age of their twenty-first birthday. Since the interpretation of the financial eligibility might be the need for immediate financial assistance, this could encompass even families whose income might be as much as $600.00 per month. It was voiced that here, too, rather rigid and strict interpretation be outlined as eligibility requirements for financial acceptance.

Dr. Vinje, in the discussion that followed, stated that it was his feeling that an excessive number of people were taking advantage of the present system. He felt that in many cases, hospitals were advocating the use of Crippled Children's Services in order to be assured of payment. He further said that the program, at the county level, was still somewhat lax in both processing and ruling on financial eligibility of the applications.

Dr. Miles indicated that problems of a minor nature, which did not require an excessive expenditure of funds, should be eliminated from Crippled Children's Services consideration. He also felt that there should be further qualification on the part of certain congenital or developmental defects to assist in determining medical eligibility for Crippled Children's Services.

It was brought to the attention of the Committee by several members of the Committee that often when the family is informed of the approximate cost of treatment, that they would then be willing to assume all financial responsibility. To assist in determining whether or not a Crippled Children's Services application would be necessary, the assistance of the physician to use reasonable judgment as to eligibility, original cost, severeness, and length of care would be of assistance in the planning by both the family and the County Welfare Board.

It was requested by Dr. Miles that the most recent list of diagnostic sheets be forwarded to each member of the Crippled Children's Services Committee.

The Chairman indicated that classifications should be made at all levels of the program with numbers listed and diseases named to assist in proper medical evaluation so that acceptance or non-acceptance can be better made at the county level. He further recommended that he felt that the speech and hearing program at the Elk's Youth Camp which had been previously reported on at the two preceding meetings, should be continued since it appeared to be functioning very well and serving a worthwhile purpose.

The Committee further felt that when patients were referred to such institutions as the Rehabilitation Center at the University of North Dakota, that the medical authorities in those institutions should be more cognizant of the interest on the part of the physician hoping for more frequent progress reports.

There being no further business, the meeting was adjourned at 11:00 A.M.

Respectfully submitted,
(Signed) PAUL L. JOHNSON, M.D., *Chairman*
Committee on Crippled Children

Committee on Mental Health

The Mental Health Committee has held no meetings during the year following the last Medical Association meeting. The explanation for this is that, in general, the committee is more active during the years prior to the legislative session, and it will be anticipated that we will be involved again in consideration of pending Mental Health Legislation. Many members of the State Medical Association have been actively engaged in the Governor's Task Forces on Mental Health and Mental Retardation which have been meeting the past year. Society members have been active as chairmen and members of these committees, and they have contributed a great deal in adding their views of their collective experiences. They have been helping to educate some of the other professional and lay groups within the state, and have made suggestions for planning in both the areas of Mental Health and Mental Retardation. As a result of these Task Force endeavors, it is apparent that a number of legislative recommendations are being made for the improvement and expansion of these programs within the state of North Dakota.

This past year has seen the first Community Mental Health Clinic established in Grand Forks and plans are now in progress for establishment of additional Mental Health Centers in both Bismarck and Fargo. In all of these communities physicians have been actively participating in studying the needs and in making plans for the establishment of these centers. The next legislative session will have to consider some revision of the Community Mental Health Center Law to make it clear that the intent of the law was that all counties and population areas could participate. The law had the intent of preventing such centers from being established in communities too small to support them. Other legislative areas that are being considered are some revision of the laws governing the operation of the State Hospital and removing from the Criminal Laws the penalties imposed for attempted suicide. There will be a recommendation for a commitment procedure by certification of one physician, such commitment to be used at times when the Mental Health Board cannot meet in sufficient time to facilitate emergency type commitments.

In March of this year, Dr. Amos of the State Health Department and your Chairman were able to participate in the AMA Conference of State Mental Health Representatives at which time a number of subjects of interest in our state were discussed. This included the possibility of a regional type congress of mental health patterned on the AMA's two previous National Congresses. Also discussed were the effects of Medicare on the care of the mentally ill and the regulations and rules set up under the Medicare Laws. Another topic of discussion was the comprehensive Community Mental Health Center.

It is encouraging that a number of District Medical Societies have established their own Mental Health Committees who are working in cooperation with local agencies on questions of Medical Society cooperation in the areas of Mental Health and Mental Retardation.

Respectfully submitted,
(Signed) ALBERT C. KOHLMEYER, M.D.,
Chairman, Committee on Mental Health

Committee on Aging and Rehabilitation

During the year 1965-1966 the Committee on Aging and Rehabilitation of the North Dakota State Medical Association met twice. All members of the Committee participated in the first meeting. The first meeting was a telephone conference on December 1, 1965.

The second meeting was on December 4, 1965. On that date members of the Committee (Donald Lamb, M.D., Brian Briggs, M.D. and the Chairman); Donald Barcome, M.D., Director of the Medical Rehabilitation Unit of the Medical Center of the University of North Dakota; Mrs. Eugenia Burr, R.N., Cass County Public Health Nurse; and Miss Connie Blackstead, Program Director of the North Dakota Broadcasting Company, Inc., prepared videotapes concerning the Stroke Syndrome. Each tape was a one-half hour program. Part 1 of the Stroke Syndrome was presented statewide through the courtesy of the KX Television Network of the North Dakota Broadcasting Company on January 10, 1966; Part II, on January 30, 1966; and Part III, on February 6 and 13, 1966. Parts I and II were panel discussions by the above-listed participants concerning cause, effects, treatment, and prevention of strokes. Part III was a demonstration of the services available and results obtained with patients at the Medical Rehabilitation Unit of the Medical Center of the University of North Dakota.

These programs were well received by the public in general. The programs were quite successful in accelerating one of the present projects of this Committee, that is, increased utilization of the Medical Center Rehabilitation Unit. As a result of these programs, there have been many referrals to the Medical Center Rehabilitation Unit. In fact, there is now a waiting list for patients at this medical facility.

Respectfully submitted,
(Signed) Harold W. Evans, M.D., *Chairman*
Committee on Aging and Rehabilitation

Liaison Officer to the North Dakota State Bar Association

No joint meeting or official business was carried out between the North Dakota State Bar and this Liaison representative from the State Medical Association. However, Mr. Burke of Grafton, who is the Chairman of the Interprofessional Relations Committee, will be getting his Committee together to meet at a proposed meeting here in Bismarck, at which time it is hoped that these state committees can be encouraged and motivate increased interprofessional activity and understanding of our interprofessional code between the local state medical and bar association groups. It is felt that these local associations could then carry on a more interesting program which would be participated in by a greater number of physicians of our respective groups.

Respectfully submitted,
(Signed) Paul L. Johnson, M.D., *Representative*

Committee on Pharmacy

It is the feeling of your Chairman that there are still a lot of unresolved problems existing between pharmacists and doctors. It is not necessarily the function of organized medicine to initiate discussion of these problems; on the other hand, doctors should have a direct line of communication with pharmacists in order to have a full understanding of the problems confronting both organizations.

It would be advisable for this Committee to meet at least once a year at a set date and not wait for a crisis before a meeting is called.

Respectfully submitted,
(Signed) O. A. Sedlak, M.D., *Chairman*
Committee on Pharmacy

Committee on Emergency Medical Service

This committee did not meet in the past year, but the following were accomplished through its liaison:

1. The State Health Department of North Dakota continues to foster the Medical Self Help Program, and the committee notes its success throughout the state, with classes concerning this program and also its accomplishment in the high schools. Dr. Amos, Mr. Robert Freise, and Mr. Anderson of the North Dakota State Health Department are to be commended on this activity.

2. A yearly exercise of the ECDH Hospital function for the sophomore medical students and ten hours of indoctrination in the Medical School on emergency medical care in conjunction with the 311 General Hospital Reserve, Grand Forks Section.

3. Full participation in teaching in medical function executed by the senior students.

4. Encouragement of the committee for a symposium on "emergency medical care" by the University Medical School under the direction of John Vennes, Ph.D., under the Federal MEND Program.

5. Assistance in the annual presentation of this program in the month of March, yearly, with an invitation and attendance by representatives of two provinces of Canada, and local hospital administrators and personnel.

Because of no business being presented by members of hospitals in the state of North Dakota, it was not felt necessary for this committee to meet in this past year.

Respectfully submitted,
(Signed) Ralph E. Mahowald, M.D.,
Chairman

Committee on Liability Insurance

There has been no meeting of this Committee and I feel there is not much purpose in continuing such a committee.

I do not think we can accomplish anything on a state level on liability insurance.

Respectfully submitted,
(Signed) Joseph Sorkness, M.D., *Chairman*
Committee on Liability Insurance

Committee on Constitution and By-Laws

No formal meeting was held by this Committee throughout the past year, but the members of the Committee were polled in regard to two matters of business referred to our Committee.

The first of these being the referral of Resolution No. 13 from the last meeting which would, in essence, amend the By-Laws to allow the number of delegates allotted to each Society to be based on the number of paid-up members at the end of the preceding calendar year. It was the feeling of the majority of the members of the Committee that they would not be in favor of this Resolution as it would do away with the present system which tends to encourage payment of dues prior to the annual meeting. So, this Committee would not recommend the adoption of this Resolution.

Secondarily is the idea of establishment of the Commissions as a replacement for the present Committee system.

Commission on Medical Service: Covering

A. Medical Economics and Governmental Agencies
B. Emergency Medical Service
C. Foreign Trained Physicians
D. Crippled Children
E. Aging and Rehabilitation
F. Liability Insurance
G. Mental Health
H. Public, Rural and School Health

Commission on Scientific Medicine: Covering

A. Scientific Program
B. Arrangements for Annual Session
C. Medical Education
D. Nursing Education
E. Cancer
F. Diabetes
G. Cardiovascular Disease

H. Multiple Sclerosis
I. Maternal and Child Welfare

Commission on Communications: Covering
A. Public Relations
B. Official Publication
C. Necrology and Medical History
D. AMA-ERF
E. Physician's Placement Service
F. Constitution and By-Laws

Commission on Allied Organizations: Covering
A. North Dakota Hospital Association
B. North Dakota Pharmaceutical Association
C. State Bar Association of North Dakota
D. North Dakota State Dental Association
E. Woman's Auxiliary
F. Medicine and Religion
G. North Dakota State Nurses Association

Commission on Legislation and Governmental Relations: Covering
A. Legislation
B. Crippled Children's Services
C. Medical Center Advisory Council
D. Governor's Health Planning Committee
E. State Health Council

It was the feeling that this Commission system merited certainly further investigation and discussion by the Reference Committee reviewing this report and possibly the House of Delegates as a whole. If it was also the feeling of other members of the Society that this Commission system should be instituted, then this Committee in the future could very well go ahead with the preparation of changes in the Constitution and By-Laws to institute these changes.

Respectfully submitted,
(Signed) KEITH G. FOSTER, M.D., *Chairman*
Committee on Constitution and By-laws

Liaison Committee to the North Dakota Dental Association

There is no new activity concerning this Committee to report at this time.

Respectfully submitted,
(Signed) DAVID G. JAEHNING, M.D.
Representative

Committee on Cardiovascular Diseases

The Committee on Cardiovascular Diseases held no meetings during 1965.

Respectfully submitted,
(Signed) ROBERT D. STORY, M.D., *Chairman*
Committee on Cardiovascular Diseases

Medical Advisory Committee to the State Highway Department

The first meeting of the Medical Advisory Committee was held at Fargo, December 12, 1965. This being a new Committee, it was outlined to the members as a tentative guide line suggested by the Safety Responsibility Division of the North Dakota State Highway Department. Their hope was that this Committee could provide the drivers' license administrator with sound medical advice concerning the licensing or the removal of licenses to special risk drivers. This would include the physically handicapped, those with mental problems, chronic conditions, and especially those individuals suffering lapses of consciousness or control.

The committee will work on suggestions to the Department of some criteria and standards to be used in determining when an individual with certain conditions should be required to submit to a medical examination to determine his qualifications to be a driver. Also some basic principles which could be applied by the drivers' license department in determining a driver's limitations based on medical factors.

Since this was the first meeting of the committee, only the establishments of guide lines was possible and much work is left to be done in the future. It was felt that basically one of the most important functions of this committee would be to obtain the cooperation of Doctors throughout the State with the Highway Department. The Chairman would appreciate the support of the House of Delegates in requesting the Physicians of North Dakota for this cooperation. One of the greatest causes of death, especially of our youths, is on the highway. As responsible physicians, it is our moral duty to help prevent these accidents.

Those present at the meeting besides the Committee were as follows: K. J. Kucera, State Highway Department; P. L. Owens, M.D.; J. D. Craven, M.D.; J. R. Amos, M.D.; J. Sherwood Williams, Field Services Division, AMA; Lyle A. Limond; and Myrtle Kohler, Recording Secretary.

Respectfully submitted,
(Signed) R. W. MCLEAN, M.D., *Chairman*
Medical Advisory Committee to the State Highway Department

Report of the Representative to the Crippled Children's Services Division Public Welfare Board of North Dakota

A meeting was held November 13, 1965 at Bismarck, North Dakota. The following members were present: Drs. J. R. Amos, Bismarck; James A. Barnes, Minot; J. J. McLeod, Grand Forks; F. D. Naegeli, Minot; G. E. Tolstedt, Bismarck; and Donald E. Skjei, Williston. Also present were: Dr. P. W. Freise, Mr. Leslie Ovre, Mr. Gottfried J. Kuhn, Mr. T. H. Tangedahl, Miss Margaret Lister, Eldean Enge, Ellen Washlund and Phyllis Wigen.

Topics of discussion were as follows:

1. Method of informing parents of newborns with congenital defects of Crippled Children's Services. Dr. Freise stated that the State Office was considering whether a letter should be sent to the parents of a child born with a defect, informing them of Crippled Children's Services as a matter of information but not soliciting applicants. It was decided that such a letter should not be sent to the parents.

2. Speech therapy—The North Dakota Crippled Children's Program was considering the expansion of their program to include provision of speech therapy for (A) Children with speech problems associated with a hearing loss. (B) Children with cerebral palsy. (C) Children with speech problems associated with mental retardation. It was decided after discussion that provision of speech therapy for all children under seven years of age who are referred by a specialist authorized by Crippled Children's Service would be provided.

3. Dental problems associated with a medically eligible condition—It was decided that the dental problems resulting from a diagnosis coming within the medical scope of Children's Services Program should be included and the provision made for general dentistry in these instances.

4. Patients who are physically helpless but not requiring technical medical care—After discussion it was decided that there would be merit in offering technical medical care to an individual on a limited basis when recommended and defined by the attending physician and to be provided in lieu of hospital care. It was thought that this would reduce overall costs as compared to hospitalization for these patients, but it was also mentioned that it would be difficult to find properly trained personnel to be available to provide this service.

5. Listing of cardiologists as specific specialty—It was decided not to list doctors as cardiologists inasmuch as there are not sufficient cardiologists in North Dakota. It was decided to leave the policy as it is at the present, that is, the referrals to any authorized pediatrician or internist depending on the age of the individual involved.

6. Inclusion of branchial cleft cyst in Crippled Children's Service coverage—The group favored including branchial cleft cyst and congenital hypoplastic anemia in Crippled Children's Services. It was decided that the medical director should have some leeway in making decisions as to medical eligibility. It was the thinking of the group that situations such as this be left for individual or public welfare board consideration.

7. Limitation of category "deformity of joints, club feet and club hands"—Dr. Freise explained that this item had been placed on the agenda inasmuch as there was a question if the category "deformity of joints, club feet and club hands" should be qualified such as "severe" or "mild" as some comparatively minimal cases are now being approved. It was decided that this specific category could be designated as "severe" or "mild" but there was a question as to whether this would be an answer to the problem. Further discussion was whether Crippled Children's Services should pay for shoes in respect to bracing. No definite decisions were made in this respect.

8. Anomalies of the bladder neck or ureters—Dr. Freise stated that the category as presently included under Crippled Children's Services is defined as "strictures of the bladder neck or ureters" and that there had occasionally been application for children with congenital abnormalties which do not fall under this definition. He proposed changing the category to "Anomalies of the bladder neck or ureters" in order that it would be more inclusive. It was agreed that this change in wording be done.

9. Rheumatoid arthritis—Question under discussion by the group was whether coverage of the acute rheumatoid arthritis should be included. At the present time the treatment of deformities of arthritis are included. It was decided that the dividing line be drawn at the point that the child is referred to the orthopedist for care.

10. Care by family physician or general practitioner—Discussion was carried on as to the ways that the specialist is aware of provision that he can refer the child back to the family physician or general practitioner for post operative or follow-up care. This had been performed by article in the Journal-Lancet and the information had been included in a periodic newsletter sent out from the State Medical Association to all member physicians in North Dakota. There followed some discussion as to the proper referral to in-state specialists and also out-of-state referrals.

11. Orthodontal and dental fees—This discussion got into fees in general and it was decided that any change in fees would follow after the meetings of the Medical Economics Committee of the State Medical Association and this would be particularly applicable to a time following July 1st after the institution of a new government program. It was decided that practitioners other than physicians should be working at the same percentage reduction as physicians.

12. Change from a fall meeting to a spring meeting—This is going to be attempted at the same time as the State Medical Association meeting is held in Fargo from April 29th to May 1st.

Respectfully submitted,
(Signed) DONALD E. SKJEI, M.D.,
Representative

NORTH DAKOTA STATE ADVISORY COUNCIL for HOSPITAL AND RELATED CONSTRUCTION

Two meetings were held during the year with representatives from: Catholic Rural Life Conference, State Legislature, North Dakota State Tuberculosis and Health Association, North Dakota Farmer's Union, North Dakota Homemakers, University of North Dakota Division of Vocational Rehabilitation, Lutheran Hospital and Homes Society, State Hospital Association, State Nurses Association, North Dakota Farm Bureau, and Congress of Parents and Teachers.

These meeting were held on June 29, 1965, and November 19, 1965. Consideration was given to various projects involving construction, replacement, addition to or modification of hospital, nursing home and rehabilitation facilities in the state.

The projects supported by the council were: Psychiatric addition, St. Joseph's Hospital, Minot, N.D.; Missouri Slope Lutheran Home, Bismarck, N.D.; Replacement Bottineau Hospital; Addition Jamestown Hospital; and Modification, Crippled Children's Hospital, Jamestown, N.D.

Summary of Federal Funds allocated and expended for Hospitals and related facilities as of November 1965

GENERAL HOSPITALS	*Federal Share of Costs only*
1. Estimated cost of completed construction and/or equipment of 34 new hospitals including replacements and additions	$ 5,722,918.60
2. Estimated cost of 2 general hospital replacements under construction at Crosby and Dickinson	$ 1,658,752.37
CHRONIC DISEASE HOSPITALS	
1. Cost of completed construction and equipment of one 60 bed facility at Valley City	$ 221,494.81
2. Cost of completed chronic disease unit of 43 beds at Trinity Hospital, Minot	$ 306,451.25
3. Cost of completed 26 bed chronic disease unit at St. Luke's Hospital, Fargo	$ 268,590.62
MENTAL HOSPITALS	
1. Cost of completed construction and equipment of a 204 bed receiving and treatment unit at State Hospital, Jamestown	$ 318,133.70
2. Cost of completed 28 bed psychiatric unit at St. Alexius Hospital, Bismarck	$ 257,971.50
3. Cost of completed 80 bed neuropsychiatric unit at St. Luke's Hospital in Fargo	$ 621,000.00

	Federal Share of Costs only
4. Estimated cost of a 32 bed psychiatric unit under construction at St. Joseph's Hospital, Minot	$ 477,381.65

SCHOOL OF NURSING RESIDENCE

1. Cost of completed residence and training facility for 150 student nurses in connection with St. Luke's Hospital in Fargo	$ 348,915.85
TOTAL	$10,201,610.35

AMENDED PROGRAMS

Nursing Homes—

1. Cost of 8 completed nursing homes at Bismarck, Dickinson, Fargo, Grand Forks, Jamestown, Mayville, Minot, and New Rockford	$ 2,226,086.50
2. Estimated cost of completed 32 bed nursing home addition at Minot Lutheran Home	$ 165,740.74
3. Estimated cost of completed 42 bed nursing home at Bowman	$ 260,917.98
4. Estimated cost of a 50 bed nursing home under construction at Northwood	$ 296,864.54
5. Estimated cost of an 80 bed nursing home scheduled for construction at Bismarck	$ 498,145.04

Rehabilitation and Treatment Units—

1. Cost of completed outpatient rehabilitation facility at the University of North Dakota Medical Center	$ 159,563.45
2. Cost of completed inpatient rehabilitation facility addition at the University of North Dakota Medical Center	$ 240,986.27
3. Cost of completed rehabilitation facility extension at Jamestown Crippled Children's School	$ 108,283.34
4. Cost of completed rehabilitation facility expansion at Jamestown Crippled Children's School	$ 111,991.09
5. Estimated cost of rehabilitation facility under construction at Jamestown Crippled Children's School	$ 170,968.20
TOTAL	$ 4,239,547.15

Respectfully submitted,
(Signed) M. A. K. Lommen, M.D., *Member*
North Dakota State Advisory Council

REPORT OF REPRESENTATIVE TO MEDICAL CENTER ADVISORY COUNCIL SPRING OF 1966

The Fall of 1965 freshmen class was the largest ever admitted. Forty-five new students were admitted, anticipating the usual three to five withdrawals or failures but none occurred. This, together with four admitted from the Graduate School and repeating previous work, resulted in a second semester class of forty-nine and undesirable overcrowding.

So far, we have fifty-seven applicants from the State of North Dakota for admission in the Fall of 1966, and forty-four of these appear to be acceptable.

We have 1,213 requests for application blanks from nonresidents so far for the Fall of 1966 class.

Of the forty-two who transferred two years ago, six graduated with honors from their transferring school, one failed, and two barely passed.

There are fifty-one graduate students. Nine in anatomy, twenty-six in biochemistry, eleven in microbiology, five in physiology-pharmacology. Twenty-one of these are on Federal grants with stipends of about $2,200 each.

Faculty

There have been no more than the expected number of changes among the faculty, and these have been adequately replaced. We have been fortunate in obtaining Dr. Russell H. Wilson to head the Department of Physiology. Dr. Wilson has an M.D. and a Ph.D. degree in physiology and is a Diplomate of the American Board of Internal Medicine. He is particularly interested in pulmonary function. There have been other additions in the physiology-pharmacology department, in microbiology, anatomy, and in pathology.

It has been the policy to maintain the faculty salary schedule at approximately the national median. This has required continuous increases in salaries, and again we find ourselves below this level so further increases will be necessary.

Space

Attempts to take as many undergraduates as possible, encourage the post-graduate training program, and add adequate faculty with space for offices and research have resulted in serious overcrowding. Whereas eight years ago, there were fifty-four faculty, staff, technicians, etc., there are now 120 in addition to the regular students, all requiring desk and laboratory space. There have been discussions with the State Health Department administrators regarding the possibility of the Public Health Laboratory transferring to more adequate quarters. Nobody desires such a change, but some such arrangement may become necessary.

Psychiatric Training Program

There have been five psychiatrists trained under this program, a number of whom are already back in the state and others, we understand, are returning next summer. Two social workers will complete training in 1966 and 1967 and one psychologist is in training and will return in 1967. The cost of all this will be about $84,800. Whether or not this program will be continued is a question at this time because of lack of funds.

Student Loan Fund

This program continues but is in less demand than a few years ago due to the AMA, Government, and other loan funds. We still have nearly $500,000 of mill levy funds tied up in these loans to medical students and dentists. The interest on the loans is just about balancing the forgiveness features of the loan program.

Dean Harwood has done an interesting study regarding the possible effectiveness of this program. While the number of graduates returning to the state appears to be increasing somewhat, a study of the graduates from 1950-1955, which was just before the Student Loan Program was instituted, found that 30 percent of the graduates of those five years returned to the state to practice while from 1956 to 1960, the first five years of the loan program, 32 percent returned. Thus the results of the forgiveness feature of the loan to encourage graduates to return to the smaller communities of the state has been unimpressive from this point of view.

Rehabilitation Center

Dr. Donald Barcome, the Director of the Rehabilitation Center, seems well versed in all phases of rehabilitation. It appears to those of us who have had an opportunity to observe the work done at the Rehabilitation Center that the work is of high caliber and merits your confidence.

There has been a marked increase in the number of both outpatients and inpatients. As of this writing, the census of inpatients is at about capacity, and there is a waiting list for admission. This increased work has resulted in increased need for personnel so that the cost of operation has increased along with income. In 1965 50% of the expenses of operation were met by income whereas to that 25% was met. The national average for rehabilitation centers is 70% of costs covered by income. The per diem charge of $25 has been substantially under cost and is lower than the cost of operation of general hospitals in the state. Accordingly, there has been a recent increase in per diem fees to $35 for inpatient care including all services, and an increase in outpatient treatment fees.

What the effect of the Medicare program on the demand for rehabilitation services will be is not known, but it is anticipated that the demand will increase.

College of Nursing

The enrollment in this school continues to increase. There are now thirty-seven seniors, forty juniors, seventy sophomores, and one hundred freshmen for a total enrollment of 247. On the basis of the past gradual increase, it is projected that by the 1968-1969 year there will be fifty seniors, sixty juniors, eighty to ninety sophomores, and 120 to 125 freshmen or a total enrollment of 310 to 325. We understand there is some consideration of closing the St. Joseph's School of Nursing of which St. Michael's Hospital in Grand Forks is a part. What effect this might have on enrollment and teaching service load at the Medical School is not predictable.

Finances

The mill levy has not been adequate to support the Medical Center for a number of years, and the surplus which was built up in the past has been largely used. About half as much money is being obtained through various grants as is being obtained through the mill levy. The accountants tell us that the critical period will arrive in the summer of 1967. It will probably be necessary and advisable that additional funds be requested from the next State Legislature.

The movement to abolish earmarked funds for state facilities and programs appears rather strong. The Committee on Constitutional Amendment of the Legislature favored the abolishment of the mill levy fund for operation of the Medical Center by a vote of 29 to 1. Accordingly, it may not be wise to further oppose the loss of the mill levy as it will be necessary to request funds from the Legislature anyway.

Respectfully submitted,
(Signed) PHILIP H. WOUTAT, M.D.
Representative to the Medical Center Advisory Council

REPORT OF REPRESENTATIVE OF BLUE SHIELD BOARD OF DIRECTORS

It was very opportune for the House of Delegates to have resolved to study and act upon a report from their representative for the Board of Directors of North Dakota Blue Shield, since this year the North Dakota Physicians Service became carrier for Part B of the Medicare Act. The North Dakota Physicians Service is now a financial agent for the payment of physician fees in the following Federal Programs: (1) Federal Employees, (2) Vista and Job Corps, and (3) Medicare for the Aged.

It is also likely to become the financial agent for the old age assistance portion of the welfare program, as outlined in Title 19 of the Medicare Act.

In addition, enrollment in the Plan at the end of 1965 was about 207,000 persons, or 32.8% of the population of North Dakota, and ranked 14th in the United States by percentage of State population enrolled. Recertification of subscribers income was completed in 1965 and 73% of subscribers have certified their income to the plan.

In spite of a planned deficit during the year 1965, the income and expenses were almost equal, and the reserves remained equal to about 4.5 months of claims and overhead expense. Several new programs were instituted during the past year, including: (1) A major medical program in groups of 10 to 25 with a 20% surcharge. (2) Increased benefits for nervous and mental illness under the Major Medical Rider. (3) Cost of living payments to participating physicians were increased to 6%. (4) Physicians are now required to sign claims submitted for their services. (5) A major medical and supplementary type of coverage has been developed to complement the coverage to be given in Part B of Medicare. (6) The Blue Cross–Blue Shield joint Operating Agreement was renewed with the agreement to rent space in a new office building to be constructed by Blue Cross. A one-year cancellation clause is included.

Several important items of business of the Board of Directors of Blue Shield have been deferred and will come up for action during the coming year. (1) Adjusted fees for psychiatric services. (2) Catastrophic illness contract. (3) Extended coverage for radiation therapy. (4) Changing maternity waiting period to date of conception. (5) Elimination of $1,000 maximum on related surgery. (6) Elimination of the 365 day limit on in-hospital medical coverage. (7) Development of a Utilization or Review Committee. (8) Increased obligation for payments to Radiologists and Pathologists now being made by Blue Cross. (9) Increasing age of coverage for children attending college. (10) Expansion of Executive Committee of the Blue Shield Board of Directors.

One major proposal for a change in the fee schedule was defeated. This was a motion proposing that when the cost of living index increases or decreases by 5% this be added to or deducted from the conversion factors under the present Relative Value Schedule.

In several areas the Board of Directors of Blue Shield are awaiting decisions from the North Dakota Medical Association. In the following areas specific action by the House of Delegates is necessary: (1) A directive indicating whether reimbursement to participating physicians in North Dakota Blue Shield be made by a revised fee schedule or totally on the basis of usual and customary fees. (2) Whether North Dakota Blue Shield should continue the philosophy of trying to help low income groups or abandon this philosophy. (3) Whether North Dakota Blue Shield should provide a major increase in fees to participating physicians, thus requiring a premium increase to the subscriber of almost double the present premiums, or whether modifications in the present fees be made in areas of inequity with only a minor increase in premiums to the subscriber. (4) Implementation of a utilization review committee and of a claims review committee by the North Dakota State Medical Association.

On the basis of the facts at hand, your representative recommends the following actions in response to the above: (1) Reaffirmation of the philosophy of trying to help low income groups prepay medical costs on a private basis. (2) Modification of the present fee schedule with respect to such inequities as are indicated by the Committee on Medical Economics and with a specific recommendation that cost of living index charges be added to or deducted from the conversion factors in the event of each change of 5%. (3) Recognizing that D plan of Blue Shield provides for the payment of usual and customary fees, accept a modified version of the present fee schedule and urge negotiations with Medicare be made on the basis of the D plan. (4) Take leadership in the development of a Utilization Review Committee with representatives from Blue Cross, Blue Shield, the North Dakota Hospital Association and the North Dakota State Medical Association, and develop a Blue Shield claims review committee from the North Dakota State Medical Association.

The Board of Directors of Blue Shield is composed wholly of elected representatives, all of whom are members of the North Dakota State Medical Association. The Blue Shield has been recognized as the fiscal agent for the payment of physicians' fees in the State of North Dakota by the Federal Government, rather than a private insurance company.

The fact that we have elected representatives negotiating for us in the matters of economic reimbursement for our services in those Federal medical programs being forced upon us, speaks highly for the wisdom and foresight of those amongst us that founded the North Dakota Physicians Service and for those who have so carefully nurtured and developed it through the succeeding years.

Respectfully submitted,
(Signed) Lee A. Christoferson, M.D.,
Representative of the House of Delegates to the Board of Directors of Blue Shield

REPORT OF THE DELEGATE TO THE AMERICAN MEDICAL ASSOCIATION

Who can argue that the immediate past and present is not one of the most important periods through which American medicine has lived? Seldom has a deliberative body in formal session found it so necessary to dwell on one topic (P.L. 89-97) so extensively as did the House of Delegates of the AMA at its two regular meetings and two special called sessions during the year 1965.

Prior policies and declarations of the AMA categorically affirmed that (1) the health of the patient came first, and (2) physicians are the best judges of what is best for the patient and of the means to attain optimum results. It must be said, too, that the AMA House of Delegates never accepted the certainty that this legislation was inevitable and that physicians should join in it in an effort to guide it. Rather, the House is on record as consistently voting to use all possible ethical means to prevent the enactment of Medicare with its overtones of compulsion, control and dictatorship. This was your delegate's feeling, also.

An initial special meeting in February in Chicago approved the "Eldercare" program as a more realistic alternative to Medicare legislation. Subsequently, much effort and many dollars were expended to promote this more acceptable alternative. The annual meeting in New York in June considered 76 resolutions with minimum controversy and discussion excepting those dealing with Medicare, wherein discussions were long, heated and varied. The House distilled a resolution which reaffirmed earlier statements of principle, called for conferences with federal authorities to assure high quality medical care for the patient and set the stage for the appointment of representative physicians to advisory committees for all federal health programs. The question of whether to participate was not clearly resolved, but precipitous and premature action was avoided and the stage set for a calm study by the delegates of the Medicare law Congress might enact—primarily, to determine whether it was a law physicians could live with in good conscience, consistent with the principle of ethics. Medicare became law! A special meeting was called in October in Chicago primarily to resolve whether nonparticipation was desirable, legal and moral.

Previously adopted principles of medical ethics and responsibilities were reaffirmed, and it was concluded that "individual physicians acting independently and not in concert with others can lawfully refuse to accept any person as a patient who is a beneficiary under the program, or he may elect to treat such a person." Although there was some sentiment in the House for nonparticipation, the consensus was overwhelming to work in our advisory committees to H.E.W. in attempting to draft rules and regulations in keeping with medicine's philosophy and interest. The Clinical Meeting in Philadelphia in December documented much of the liaison work already accomplished between medicine's representatives and H.E.W. I sensed a feeling of watchful anticipation on the part of our advisors to H.E.W.; however, a dialogue had been established and apparent good faith was manifest on both sides.

Of prime interest to North Dakotans was the candidacy of our own Dr. Willard Wright for the office of President-Elect of the AMA. That Willard was more than seriously considered for this high honor by his peers is indicative of the high esteem in which he is held by those in the House with whom he labored so many years. Power politics prevailed and Dr. Chas. Hudson of Cleveland was elected to this office. Willard did not lose stature in this effort. He remains a key member of the powerful and influential Council on Medical Services, a recent delegate to the World Medical Assembly and a member of one of medicine's advisory committees to H.E.W. A grand total of 64,517 persons including 24,268 physicians registered at the New York meeting. The fact that the Meeting of the House attracted probably no more than 1,000 persons including the delegates serves as a reminder that the scientific program of the Association is still the main interest of this country's physicians, and that it serves this interest with personnel and resources many times greater than that allotted to its much publicized, infrequent and essential political activities.

It is not possible nor necessary to detail all the actions at these meetings. They are adequately covered in AMA publications, including the AMA News which should be read by members of the North Dakota House of Delegates. Some idea of the volume of problems and issues to be dealt with can be had from the Philadelphia meeting where there were 65 resolutions presented as well as 15 supplementary reports to the Board of Trustees and 17 supplementary reports to the Councils and Committees of the AMA. These, of course, were in addition to the annual reports published by the numerous Councils and Committees which had to be read and digested in advance of the Convention. It is apparent that the wide scope of problems which present themselves for deliberation, discussion and action could not be dealt with adequately by a lone delegate. Here and now I should like to pay tribute to the North Dakota delegation, Drs. Wright, Painter, Larson, Craven and Toomey, and Lyle Limond, for their gracious help.

Certain actions of the AMA House should be considered by the North Dakota House. (1) The AMA House approved the Board of Trustees recommendation to increase AMA dues effective January 1, 1967 from $45.00 to $70.00. This matter will come up again at the annual convention in June, and will be voted on again at that time. (2) The AMA House adopted the "usual and customary fee" concept as the basis for reimbursing physician participants in governmental programs at all levels and urged acceptance of this concept upon all third parties. (3) Recommendations for enactment of legislation to legalize abortion when medically indicated and sterilization under certain circumstances were referred to the Board of Trustees for further study and report. It was suggested that the Association and State and County Medical Societies can render a distinct public service in this matter by conferring with other interested groups such as lawyers, clergy, sociologists, legislators and government administrators. (4) A resolution urging State and County Medical Societies to "participate in public hearings in the development of appropriate standards which would assure uniform signs on our limited access highways and interstate systems indicating the location of the nearest licensed hospital." (5) Reports, adopted by the House, urged continued effort of local and state societies to provide adequate physician representation on Hill-Burton advisory councils and area-wide planning agencies and to play an active role in the stimulation and development of voluntary health facility and services planning—to initiate and help formulate community health facilities and service studies in their local areas. (6) Medical staffs and state and component medical societies are urged to encourage establishment, maintenance, and proper use of cancer registries in hospitals. (7) The AMA urges state and local medical societies to encourage widespread community development of the Explorer Scout Program for Medical Specialty Posts throughout the United States. (8) All state and county medical societies are asked to approve, where feasible, the inclusion of a voluntary, nondeductible contribution to independent political action committees in the society's annual billing statement. (9) State Medical Associations are urged to sponsor conferences on utilization to provide guidance for physicians in establishing utilization review and claims review programs at the local level.

It is the hope of the delegation to the AMA House of Delegates to somehow improve communications with our North Dakota physicians. Any suggestions as to how better implement this vital task are welcome.

Respectfully submitted,
(Signed) Thomas E. Pederson, M.D.
Delegate to the
American Medical Association

RESOLUTIONS FROM SIXTH DISTRICT MEDICAL SOCIETY

RESOLUTION NO. 1

WHEREAS any arrangement between government and a citizen whereby the government agrees to pay for the citizen's medical care does not, directly or indirectly, or by inference, involve the physician in a contract with the government, and

WHEREAS once a physician accepts a person as his patient, his primary and sole obligation, his contract and his relationship are with the patient regardless of what third party may be involved;

NOW, THEREFORE, BE IT RESOLVED that the House of Delegates of the North Dakota State Medical Association request and urge the members of this Association to deal directly and only with the patient, both in providing medical care and in billing for just and reasonable compensation for the medical care provided, and

BE IT FURTHER RESOLVED that in accordance with the principles of medical ethics, that each and every member of this Association submit to the patient his own bill and receive on his own behalf, compensation for his professional medical services.

RESOLUTION NO. 2

WHEREAS hospital based medical specialists (Physiatrists, Radiologists, Pathologists, and Anesthesiologists) are engaged in the practice of medicine, and

WHEREAS the services of such specialists should not be merged with hospital charges,

NOW, THEREFORE, BE IT RESOLVED that the House of Delegates of the North Dakota State Medical Association subscribes to the principle that the charges of such specialists should be established, billed and collected by the Medical Specialists in the same manner as are the fees of other physicians.

COMMITTEE ON MEDICINE AND RELIGION

The Committee on Medicine and Religion has been relatively inactive on the state level during the past year. It is hoped that the local Committees on Medicine and Religion have been using the material and the planning we have done from the previous years to get their local programs established.

We are finding it difficult to arrange meetings of the state committee because of conflicts and poor attendance. One meeting was held in Bismarck on March 26 at which time Mr. Ethridge of the AMA, Department of Medicine and Religion, met with us. The meeting was devoted to discussion of plans for further implementing the activity on the local level. Tentatively, we are considering more emphasis on regional and local meetings than any statewide meeting because of the distances involved in statewide meetings.

Mr. Ethridge plans to be in attendance at the State Medical Meeting and hopes to contact local medicine and religion chairmen at that time.

Respectfully submitted,
(Signed) M. J. E. Johnson, M.D., *Chairman*
Committee on Medicine and Religion

This completes the Committee reports, which were assigned to the various Reference Committees.

SPEAKER'S ADDRESS

Speaker Christoferson next introduced Mr. J. Sherwood Williams of the Field Service Division of the American Medical Association.

Mr. Williams' remarks follow:

I would like to begin my comments to you this morning, by quoting to you a most important provision of law:

> "Nothing in this title shall be construed to authorize any Federal officer or employee to exercise any supervision or control over the practice of medicine or the manner in which medical services are provided, or over the selection, tenure, or compensation of any officer or employee of any institution, agency, or person providing health services; or to exercise any supervision or control over the administration or operation of any such institution, agency, or person."

Thus saith the Congress in Section 1801 of Title XVIII of the Social Security Act. It is your responsibility, as members of the medical profession, as well as the American Medical Association, to preserve the quality of medical care and the direct physician-patient relationship that the people of this country have enjoyed throughout the years. In order to do this, we must see that this provision of the law is faithfully carried out.

As you can see from this provision, it was not the intent of Congress to interfere with the practice of medicine. So our problem is no longer with the Congress but with the staff of HEW, and particularly the staff of the Social Security Administration. The only thing we can do about Congress is change some of the faces this November, but we must keep a constant vigil to see that the staff people who are the actual authors of the rules and regulations keep faith with the intent of Congress. It has been reported by the members of the various Technical Advisory Committees that they have been moderately successful in this vigil. They have won a few, and lost a few, but every effort is being made to make this law at least liveable.

There is another provision in this law that could be construed as a "saving grace." This is the provision that allows physicians under Part B a choice of methods of payment. He may bill his patient directly, and be paid directly by the patient, or he may accept an assignment and receive his payment from the fiscal intermediary. Briefly, let me review with you how this will work. If you decide to take the assignment method, you will submit your statement to Blue Shield and be paid 80% of what they have decided is the reasonable fee for the particular procedure; that is, after the $50.00 deductible has been incurred. You must then bill your patient the remaining 20%. May I remind you that you can only bill this patient for 20% of the reasonable fee as determined by the intermediary. But, if you decide to bill your patient directly, your fee may, or may not have any relationship to the reasonable fee as determined by the intermediary, but it would be a fee that you have determined to be a reasonable compensation for the service you have performed. It would be up to the patient to pay you directly, and then take his receipted bill to the intermediary for reimbursement of 80% of the intermediary's reasonable fee. Although it is not going to be as easy as all that, it would appear to me that the latter method would be the most desirable. The AMA has not made an official policy on this and from what I understand, the AMA, as an organization, cannot recommend one way or the other, because it seems that would again violate some provision of the Sherman Anti-Trust Law, but I have the feeling that the direct billing procedure is preferred by management.

I have talked to you today about these two provisions in an attempt to point out to you that there are built-in protections in the Medicare Law. Through the technical advisors, every expense is being expended to have things in your behalf.

Thank you very much for allowing me to talk to you this morning. Your very fine Executive Secretary, Mr. Limond, at your Headquarters has been very helpful to me this past year, and his staff likewise."

Speaker Christoferson thanked Mr. Williams for appearing at the meeting.

In connection with Mr. Williams' presentation, Dr. Vinje raised the following question: "It is my impression that in this particular state where Blue Shield will be the Carrier, that the patient, in order to receive the benefits under Medicare, has to present evidence of having paid the initial $40.00 or $50.00, before Medicare will accept this individual's bill? Is this true?"

Dr. Christoferson stated that this matter would be discussed at the next meeting of the House and this question would be answered at that time.

He next presented Dr. E. H. Boerth, who was the only Past State President who was present at that time.

SPEAKER: Through the years the Association has been blessed with a number of fine Presidents, and we had a particularly fine one this past year. It is my pleasure at this time to introduce to you, Dr. Joseph Craven.

PRESIDENTIAL ADDRESS

DR. CRAVEN: Mr. Speaker, Members of the House of Delegates and Guests: It has been a year since I have had the privilege of addressing this House. In the interval, I have enjoyed the opportunity to serve your Association on a variety of occasions in this State and elsewhere. I shall be forever grateful for the trust you have shown in allowing me to carry out these duties.

I have visited most of this Association's District Societies during the year and on these occasions I have expressed personal views regarding the plight of medicine in our country. Perhaps it has seemed to some of you that I have over-emphasized National Medical Problems, at the expense of our local State-wide medical affairs. It is my hope that at the conclusion of these remarks that you will agree that national medical problems and local medical problems are one and the same, with minor exceptions.

Our profession has been under a greater encompassing attack by our Federal Government the past year than ever before in our 119 year history. There has been a tendency in our country to accept this intrusion of Government into what has heretofore been the private domain of medicine, and in like manner there has been a trend in our membership, even among members who in the past have been steadfast in their adherence to the principles under which American Medicine has attained world-wide acclaim of excellence, to accept the unacceptable.

This is not a time to abandon principles but rather a time to renew and rededicate those principles. A time to regroup our forces against further onslaughts against our profession which we know are about to come.

If we concede that the inroads made into our professional independence. The birth of the AMA, 119 years ago, was brought about by a group of dedicated men whose prime objective was to upgrade and improve medical education in our country. That their objectives were attained beyond their fondest expectations is attested to by the fact that American Medicine is acknowledged by all to be the World's finest.

I would propose a quiet revolution for American Medicine. If we are agreed that total socialization of American Medicine is an evil to be avoided at all costs, and if we accept the reality that this is the objective of those who would enslave us, then certainly certain changes in our National Organization are necessary.

I would propose that the individual State Medical Societies reassess and screen their delegates to the AMA, state by state, with the objective of sending their finest as delegates to the National Organization. These should be young men, dedicated men, of principle; and yes, eloquent men. If the House of Delegates of the AMA is revitalized, all other phases of organizational medicine will inevitably benefit.

It should be unnecessary for me to note that our State, which has always enjoyed prestige and recognition at the National level far beyond that warranted by our poor numbers, is now represented by two fine men who embody all of the qualities and the leadership of which I speak. I refer to Tom Pederson and Bob Painter, of course. Unfortunately, this happy situation does not exist in all states and all too often a physician is sent to the National House of Delegates, as a delegate in his declining years as a reward for past "meritorious service." This method has worked quite well in the past, but, gentlemen, these are changing times and new approaches are needed.

There are many facets that could be enlarged upon relative to improving the effectiveness of the AMA. It is imperative that measures be taken to reunite the splinter groups that have developed within our profession. In the words of a famous American who also faced disunity, "either we hang together, or we hang separately."

Closer to home with the constantly increasing presence of third party participation in medical care, it would seem appropriate for this Society to set up a designated Mediation Committee of Appeal to arbitrate differences that will arise between fiscal agents, other third parties and the members of our Society. True, at the present time, this task falls within the duties of the Council, where it might well remain or it could be transferred to an existing committee such as Medical Economics. With increasing problems of this nature anticipated, it would seem prudent to designate and assign this important task specifically.

And, finally, I have been approached late in my term of office and am sympathetic to a proposal that this Society give serious thought and study and possibly initiate plans to establish a Medical Museum of Medical History in the Theodore Roosevelt Park. Perhaps a Special Committee could be set up for this purpose. I have been impressed by the enthusiasm and study and work that has been done by one of our members, Dr. Charles Arenson. He would make a fine Chairman for such a Committee.

In conclusion, may I offer my sincere thanks to all of the fine members of this Association who have served so unselfishly through the past year. I would solicit the same wholehearted cooperation for our new President, Dr. Toomey.

Gentlemen, it has been my very great pleasure.

Dr. Christoferson thanked Dr. Craven for his fine address and stated that the matter of the Mediation Committee was already on the Agenda and would be brought up at the next Session of the House of Delegates. He referred the matter of establishing a Museum to Reference Committee No. 2 for their deliberations.

He next introduced President-Elect, Dr. G. W. Toomey, adding that he felt the Association had chosen very well in our forthcoming President.

INAUGURAL ADDRESS

DR. G. W. TOOMEY: Mr. Speaker, Fellow Physicians: This portion of the Agenda has always seemed rather premature and presupposing to me. However, realizing full well that the Nominating Committee could go askew, and realizing that many nominations could come up from the floor, I have a few prepared remarks as required by our Constitution and By-Laws.

It is amazing what contemporary usage of a word or a phrase will do to change the meaning of that word or phrase; for example, take the word "square." In the past there was no higher compliment given a man than to say he was a "square shooter," and advertising which promised a "square deal," implied the highest integrity. This is quite in contrast to the derogatory way in which square is used today. A square today is a man who gives his employer a full day's work for a full day's pay. A square is a person who gives good service, whether or not a tip may be expected. A square is a person who shows courtesy in his dealings with his fellow men or while driving on the highways. All of these people are called "squares" by those who have lost their own individual integrity. As a result, the dictionary defines "square" as "a person rejected for conventionality or respectability." By the same token, the words "Free Enterprise" are an interesting example of the evolution of a phrase reflecting current usage. If you will look up this phrase in Webster's Collegiate Dictionaries (various publications over the past years), you will find in the 1954 edition the following definition for "free enterprise:" "The economic doctrine or practice of permitting private enterprise to operate with a minimum of control by the government." The 1959 edition has the following definition: "Freedom of private business to organize and operate for a profit in a competitive system without interference by government, beyond regulation necessary for keeping the national economy in balance." Now, if you will take the 1963 edition, "Free Enterprise" is described as "Freedom of private business to organize and operate for profit in a competitive system, without interference by government beyond regulation necessary to protect public interest and keep the national economy in balance." In other words, note that the role of government in the Free Enterprise system has changed from that of protecting the rights of individuals, to responsibility for keeping the national economy in balance, and then to the role of regulation necessary to protect public interest and keep the national economy in balance.

Public interest has been interpreted by those in government to include almost every phase of our lives. With this little prelude, let us look into the way we are affected by these changes. Some of us have heard the repeated warning, for over 30 years, and have heard it until it has become an old cliche—"Medicine is at the Crossroads." We can no longer use this term, as the turn has been made—we have passed the Crossroads and the turn has been made for us, not by ourselves. We are now working under the latest definition of Free Enterprise which includes a great deal of government regulation, as you all well know. Medicare is with us, this is only the beginning, and it is with us to stay. How far it will go, no one can predict. I'm sure many of you do not yet have the bugs ironed out of your utilization plans and committees and already we have to start preparing for more—Title XIX, and the beginning of Public Law 89-239—the Bill on Heart Disease, Stroke and Cancer. Suffice to say that how much farther we are taken into the throes of Socialism will depend partly upon ourselves. If we cannot have Free Enterprise as we have known it in the past, let us at least strive for Fair Enterprise. How are we to meet the problem?

Frankly, I do not have the answer, and I am sure no one else has the complete answer to it. However, we must resist actively and passively, and we must negotiate. All of Medicare and all of the Cancer, Stroke and Heart Disease Programs are not bad, but these programs cannot function without the doctors cooperation, so we should be in a good position to negotiate, to demand and to deliver ultimatums. It is gratifying to know we are not alone. You have all had many of your patients, the same as I, express their wish to keep their private insurance and I know some who expressed their disgust at being called long distance by a Federal Agency only to be prodded to sign up for Part B of Medicare.

In our negotiations we must be as well prepared as possible, for when we meet with government bureaus, they are well briefed and have their decisions ready and well in hand, and have done a good job with their homework. I can only consider a few guidelines which may be of help.

First of all, we must have unity within our own ranks. With government programs becoming larger all the time, there will be directives sent out from Washington and in turn, these directives will require the appointment of various committees and heads of committees within the states. It is very easy for these committees, composed of doctors, to take advantage of certain directives and use them to their own advantage and aggrandizement to the detriment of other members of the profession. Without being specific, this has happened in the past within our own state and has caused a great deal of ill feeling between various groups of physicians. I hope, in the future, anyone who has the power to direct special committees and programs will bend over backwards to see that as far as possible, all of the physicians in the state are treated equally.

Secondly, we must have a strong central organization. I have been rather distressed at times at the criticism of the American Medical Association; I have been distressed by remarks I have heard within my own local society. If we will go back through the years and look at what the American Medical Association has done, not only for us as doctors, but for the public as well, I think it deserves a great deal of commendation. It is a large organization; it's bound to be cumbersome, and being made up of human beings, it is bound to make errors at times. However, if anyone wants to really find out what the AMA does, he can go to Chicago, pay them a visit, or better yet, go to an AMA meeting and go through the drudgery of sitting through the entire meeting of the House of Delegates and spend some time at the special committee meetings in the evenings. These men are dedicated; they have worked hard and I think their resistance and foresight have staved off complete State Medicine for many years. With their recent negotiations with the Federal powers, I think they have done an excellent job for us.

Without attempting to go into them in detail, the AMA has some 80 different programs which it sponsors. These programs require the services of lawyers, accountants, physicians, chemists, economists, journalists, radio and television experts, librarians, statisticians, computer experts, etc. The budget of the AMA is some 26 or 28 million dollars a year. Only 30% of this is derived from dues. This year you will be asked to pay an increase in dues. It was interesting, at the December meeting in Philadelphia, when this increase of dues was discussed on the floor of the House of Delegates. The men from one of the large Eastern states were adamant in their refusal to go along with this increase being voted upon until the June meeting. They stated, if it were passed, they would lose more revenue from their state by men dropping out than they would gain by the increase in dues. I hope North Dakota will not be guilty of losing one member to the AMA because of a $25.00 a year increase in dues.

It is almost certain that after the meeting in June, the dues will be increased $25.00 a year, bringing the total to $70.00. This brings a little incident to mind. Going up in an elevator in a hotel, our gregarious Executive Secretary, Lyle Limond, asked the elevator girl how much dues she paid to her union each month—the answer $8.00. I am sure that if an elevator girl can pay $96.00 a year to her organization, we can afford $70.00 a year to ours. There are not enough of us, and we do not have enough money that we can afford splinter groups. So my plea, again, is loyalty to the AMA as our central organization. I know of no medical group that can be heard in Washington as the AMA can.

Thirdly, whether we like it or not, we must become more involved in politics and legislation. We, as physicians, must assist in getting the right kind of people into government. There are very few of us who have either the time or inclination to run for public office, and understandably so. However, those of our members who do, should have our wholehearted support. We can devote time to developing candidates for political office and we can give our financial support to candidates who are friendly to us. We should not get trapped into becoming associated with only one political party. It is sheer stupidity to cling to the shortsighted, outdated concept that only one party contains good people. If for no other reason it is stupid because, if we do this, we might find ourselves continuously on the outside looking in. We should devote our political efforts to backing and developing men who have high qualities of integrity, honesty and initiative and who will be friendly to us, regardless of party affiliation.

Along this line, I wish to make a plea for AMPAC-COMPACT. It was very gratifying to see North Dakota mentioned on the front page of the *Daily Bulletin* at the interim meeting of the AMA. The notice was on the front page that the awards were being given for membership and contributions to AMPAC. This was based on actual amount, and actual membership; also based on the membership and amount of donations per capita. North Dakota ranked third or fourth and received honorable mention on the basis of percentage of members of the society belonging to AMPAC and contributions per member. In view of the fact that only about 50% of our membership has paid into AMPAC, some of the states must have made a miserable showing. However, AMPAC should become stronger and I feel we should give it our wholehearted support, as it is one of our best ways of backing people who will be helpful to us.

A Legislative year is coming. Our very efficient Executive Secretary will be calling on many of you for help. You all know he has an index in his office with all of the doctors' names and their affiliations, if any, with their state Representatives or Senators. I must take some credit for this, as I first suggested this plan to Forsyth Engebretson many years ago when he was our Executive Secretary. However, the point I want to get across here is when Lyle calls you, get on the phone and do what you can with your Legislator. Better yet, when possible, get down to Bismarck, attend some of the sessions, and give Lyle some help at committee hearings whenever you can. I would like to see all of the societies follow a policy which we in the Second District have followed; that is, inviting all of the candidates for political office to one of our monthly meetings, as our guests, before the Fall election. We get to know them, they get to know us a little better, so regardless of who wins, at least we have had some contact with them before the election. We feel it has helped us some in the Second District.

I am rather perturbed with some of the men I have talked to who seem to take Medicare as a matter of course and we have, of course, the privilege of putting our heads in the sand, acting like ostriches and saying, "It will make no difference." Or, we can negotiate, and while negotiating, we can resist and try to preserve at least some semblance of Free Enterprise and have some voice in our destiny.

I would like to tell you a story which may illustrate the point I am trying to make. The story is entitled "Are Minks Like People." (This may sound like a risque story, but it is not). The story is about the mink farm in a certain area where a driverless tractor got away and cracked open the mink pens. A hundred minks, worth

$200.00 each, slipped through the holes and lit out for freedom. Ordinarily, a free mink, in his natural state, would have set up housekeeping alongside the nearest stream and started hunting, but apparently these minks had been in captivity so long, they didn't have enough gumption left to provide for themselves. Breakfast time, next morning, found many of them back in their broken pens, and by supper time, practically all the minks had returned voluntarily to captivity. I can only say that the moral of this story is that if we accept government interference and supervision without negotiation and resistance, we are substituting expediency for independence. To resist we must have unity, a strong central organization and we must be politically minded.

I wish to thank you for your confidence in me. I am sure that with my friends, old and new in the society, and with the always efficient help of Lyle Limond and his staff, we will be successful in solving our problems during the coming year.

Dr. Christoferson thanked Dr. Toomey and assured him that the members would work with him and for him to the best of their ability throughout the coming year.

The Secretary, W. M. Buckingham, was asked to read the list of the members of the Nominating Committee. The members are as follows: G. A. Dodds, M.D., Chairman, C. J. Glaspel, M.D., and E. H. Boerth, M.D.

SPEAKER: I should note at this time that the Councillors to be elected will not be nominated by the Nominating Committee. All Councillors to be elected must be, first of all, recommended by their District Society. Councillors are to be elected from the Fourth, Fifth and Tenth Districts this year. They will be elected from the list of names selected by their District Societies. Should you desire to know their names so as to make up your mind how to vote, I would suggest that you contact the Councillors. Dr. Naegeli is the Councillor for the Fourth District; Dr. Christianson for the Fifth District and Dr. McLean has been renominated from that District Society, as the only nominee from the Tenth District.

There are three items of Old Business left over to be discussed and acted upon at this meeting. The first is the matter of the study regarding Osteopaths to be represented on the State Board of Medical Examiners. You have before you a copy of a letter written to me.

Dr. Buckingham was requested to read the cover letter directed to the Speaker, dated April 22, 1966, from Drs. Nuessle and Cleary, regarding this matter and also their conclusions which follow their report, as follows:

April 21, 1966

Dr. Lee A. Christoferson
Speaker of the House
79th Annual Meeting, N.D. State Medical Association
Fargo, North Dakota

Dear Dr. Christoferson:

The 39th Legislative Assembly of North Dakota passed House Resolution 7. This was a resolution directing two members of the 39th Legislative Assembly, together with two members of the State Board of Medical Examiners, and two members of the State Board of Osteopathic Examiners, to study the feasibility of a single licensing board for both professions. Dr. R. F. Nuessle and Dr. J. W. Cleary were appointed by Dr. H. L. Reichert, who was then Chairman of the Board of Medical Examiners, to represent the Board on this committee.

A preliminary report of the committee transactions was given to the House of Delegates at the 78th Annual Meeting of the North Dakota State Medical Association in May, 1965. The House of Delegates requested us to study the problem further and to report back in one year.

The results of our study are as follows:

I. *Minnesota*

This is a direct quotation from the report of the Minnesota State Board of Medical Examiners to the House of Delegates, Minnesota State Medical Association, May, 1964.

"A law was passed at the 1963 session of the Minnesota State Legislature relating to the practice of medicine and osteopathy. A committee was appointed about 2 years prior to the enactment of the law by the governor at that time to study the problem. The committee was composed of three doctors of medicine, three doctors of osteopathy, and a neutral chairman. After several meetings and approval of the Minnesota State Board of Medical Examiners, the committee influenced the House of Delegates of the Minnesota State Medical Association and the Minnesota State Osteopathic Association in 1962 to support the legislation adopted in 1963.

As of May 1, 1963, the former Board of Osteopathy was abolished. On that date a new Minnesota State Board of Medical Examiners was created and so designated. A doctor of osteopathy was placed on the Minnesota State Board of Medical Examiners which has a membership of seven doctors of medicine and one doctor of osteopathy."

The next quote is the report of inspection visits to osteopathic colleges by the Minnesota Committee. They inspected three colleges.

"Conclusions:

1. It is the conclusion of the committee that these schools are teaching standard medical principles and practices. In doing this, accepted medical methods, text books and publications are employed. The place of osteopathic theory corresponds roughly to that of physical medicine and is being subjected to scientific evaluation. There are limitations of physical facilities and of clinical teaching material. Teaching is strongly oriented towards general practice.

2. It is the recommendation of the committee that the three schools mentioned in this report be approved by the Minnesota State Board of Medical Examiners and that graduates of these schools be admitted to the licensing examinations.

II. *Ontario*

This is a report of the College of Physicians and Surgeons of Ontario, January, 1965. The Chicago and Kirksville, Missouri Schools were inspected. The final conclusion in the report of the inspectors is as follows:

"1. No osteopathic college is a faculty of or affiliated with, a multi-faculty university. This constituted a fundamental and the single greatest deficiency.

2. The osteopathic colleges insulate their facilities from the main stream of medical progress and teaching, particularly in the clinical fields.

3. There is no uniformity in the provisions of facilities for teaching of basic sciences; at the Chicago School they are primitive and quite unsatisfactory. At Kirksville, on the other hand, they are modern and highly admirable. Although a high proportion of the basic science teachers have been trained in the graduate schools of universities in the United States, the teaching facilities in some of the departments are far inferior to those which are obtained in Canada and the programs of research, although in some instances are most admirable, lack the opportunity of offering graduate training, with the attendant stimulus to the teaching program.

4. Although in the clinic fields the faculties profess to teach principles and practices as taught in schools of medicine, the hospitals are much too small to provide the volume and variety of patients necessary for experience and training. It may be argued that the responsibilities imposed on the senior students at Kirksville provide a maturing experience which can compensate for the lack of in-hospital clinical training. This view is not likely to be accepted in Ontario. The medical libraries described, except that in Kirksville, are inadequate for the teaching and research responsibilities which should exist in schools with the number of students in the schools of osteopathy.

5. The teaching budgets are very small compared to those in Canada which reflects inability to provide: (A) Sufficient supplies and modern equipment for teaching, (B) A staff adequate to teach the large classes and to engage in productive research, (C) Salary levels which can attract teachers of the highest caliber."

This paragraph is a quote from the November, 1964, session of the Council of the College of Physicians & Surgeons of Ontario.

"In view of the conclusions of the special committee on osteopaths which are based upon the findings arrived at in the previous meetings, and upon the findings of an inspection of the osteopathic schools carried out by the specially appointed inspectors, which indicates that the quality of medical education offered in the osteopathic schools in the United States does not reach the standards obtained in Canadian medical schools; and in view of the fact that it would be entirely undesirable for the college to countenance two standards of medical education in this province: Be it resolved that the College is opposed to any revisions being made for registration of osteopaths under the Ontario Medical Act."

III. *Maryland*

The following is a direct quotation of the conclusions of the report of the Ad-Hoc Committee on Osteopathy of the Medical and Chirurgical Faculty of the State of Maryland.

"Conclusions:

1. Under the proposed changes in the law, osteopaths and doctors of medicine would take the same examination to practice medicine. Equally important, however, in granting a license to practice medicine is the knowledge of the education and training of the physician, and this can be properly evaluated in the case of doctors of medicine. In the case of doctors of osteopathy, this is not possible at this time because the Association of American Medical Colleges has suggested that it be allowed to inspect the osteopathic colleges; these osteopathic colleges have so far not allowed themselves to be inspected.

2. The committee has had correspondence with the deans of five medical schools in Philadelphia and the officers of the Pennsylvania Medical Society regarding the training of osteopaths at the Philadelphia College of Osteopathy. These physicians state that the training of osteopaths is far below medical standards.

3. The committee feels that granting a limited license to osteopaths would not relieve the shortage of general practitioners in the rural area of Maryland. The Governor's commission to study the shortage of general practitioners in Maryland concurs in this opinion.

4. It is the opinion of this committee that osteopaths must meet the same standards of education and training, as well as examination, to be awarded a license to practice medicine.

5. The deans of the two medical schools in Maryland participated in this study and concur in the following recommendation:

"The committee recommends that the medical and chirurgical faculty oppose any change in the Medical Practice Act or the Osteopathic Practice Act which would grant osteopaths licenses to practice medicine."

IV. *Nebraska*

In 1964 the Nebraska State Board of Medical Examiners was directed by the revised statutes of the State of Nebraska to conduct an inspection of all of the osteopathic colleges in the United States. Members of the inspection team included the dean of the University of Nebraska School of Medicine and the Dean of Creighton University School of Medicine. Also on the inspection committee were members of the Nebraska State Board of Medical Examiners. It was the consensus of the committee that each college did not at that time meet the minimum requirements for accreditation ordinarily applied to medical schools of the United States. The summaries and conclusions from the inspection of each college will now be quoted directly.

A. Chicago College of Osteopathy.

"The general organization of the faculty conforms to most of generally accepted practices of medical school organization. The institution is unique in that it is not associated with a parent university. Because of the relationship of the dean to the chief executive office of the hospital and of the outpatient clinics, the president is, in fact, the chief executive officer and it would appear that the dean is responsible primarily for the direct supervision of the preclinical instructional departments. There is no question but that the number of faculty members in all departments is less than the usual minimum number. This is particularly noticeable in the preclinical departments where almost without exception in the American medical school, all of the faculty are full time, and in each department are usually recruited to represent the major subspecialties of the particular basic science. This depth of faculty is lacking in both the preclinical and clinical departments. The student faculty ratio is excessive as compared with usually accepted standards. This ratio limits the amount of attention that can be given to the individual student by the faculty and since many of the faculty in the basic sciences have other responsibilities and in the clinical departments have responsibility for the care of many patients, it would seem to virtually preclude the pursuit of research which produces the stimulating environment for learning and which provides an example to the student of the scientific method which is the foundation of modern medical science.

The principal teaching hospital in Chicago does not provide teaching beds in sufficient number.

In the 1962-1963 year, the average medical school expended more than $5,000,000. Only 5 of the 87 medical schools in the United States have expenditures less than $2,000,000. It would appear that the budget of the college is less than the minimum generally considered as necessary for the successful operation of a 4-year medical school. It is generally considered not possible to find a significant profit from the operation of a teaching hospital. The reliance upon the income from the operation of the hospital and the clinic would seem to compromise the clinical instruction and to provide all too limited supplement to the tuition income available for the operation of the college. Alumni giving is above the average and is commendable. Discussion of finances with the dean or with the president seemed not to reveal any significant source of funds for the improvement of the operating budget of the college.

Student records appeared to be properly maintained. Using the usual criteria of college quality point averages and scores obtained from the student medical college admission test, it would appear that the students admitted to the college of osteopathy are definitely below the standards usually admitted to United States medical schools.

The plant appears well maintained but it is grossly inadequate for the responsibilities of the average medical school. A study of the needs of the development of new medical schools published by the Department of Health, Education, and Welfare indicates a need for more than 200,000 square feet per basic science building. The 14,000 square feet available for the teaching of basic sciences appears a significant inadequacy.

The library, by most standards, is too limited both in its collection and in its physical facilities.

The clinical facilities on the Chicago campus lack clear cut departmentalization.

The usual philosophy of clinical learning for the undergraduate student assumes the assignment to a very limited number of patients, each one of which is studied in considerable detail by the student. The student maintains a meticulous record of his findings and the reasons for his conclusions. It is the responsibility of the intern and the resident and the faculty to also record not only their findings from the study of the patient, but the reasons for each procedure in the management of the patient. There was no evidence that this approach was used in the teaching of students. The assignment of students to home calls, to collect a fee for services rendered, without the supervision of a licensed physician appears to be the exploitation of the student, and of the patient, and does not represent the supervised learning experience usually associated with clinical instruction. The rapid rotation from service to service in various parts of the clinical curriculum deprives the students of the opportunity to follow a long term course of the patients or of human illness. The hospital laboratory was small, crowded and lacked the space for significant participation of the student in the affairs of the laboratory.

The curriculum in its overall allotment of time in various subjects is similar to that employed in most schools of medicine. The clinical curriculum is difficult to analyze because of lack of departmentalized assignments and the admission that the time allotments described in the bulletin of the college are estimates. The rapid rotation of services in the clinical years is not consistent with commonly accepted educational practice.

In each of the items summarized, the Chicago College of Osteopathy does not appear to meet the minimum standards usually found in the United States Schools of Medicine. Plans for expansion of facilities and faculty may eliminate some of these deficiencies.

These deficiencies cannot be overcome at once, but may be overcome over a period of years. As yet this school of osteopathy cannot be considered capable of training students comparable to those graduates of medical schools. We must rate this college on its present merits and not on future plans. When these plans are completed and the changes made, it is recommended that this school be re-surveyed."

B. Kirksville, Missouri College of Osteopathy and Surgery.

Summary and conclusion:

"The administrative organization of the Kirksville College of Osteopathy and Surgery is generally similar to that of a 4-year medical school. There is little similarity, however, in respect to the selection of students, educational objectives and methods, teaching capabilities, research emphasis, and adequacy of medical facilities and material. There is no academic affiliation with an institution of higher learning which is traditionally and properly both the parent and the conscience of the biological sciences of which any medical school is but a subdivision.

There is a limited number of applicants compared with the average medical school. Additionally, there is a large number of applicants with a college record of less than a B average. The medical college admissions test is not required, nor do many applicants submit it with their applications. The inspection indicates that this institution is definitely less selective than an accredited medical school.

The average 4-year medical school has approximately 100 full time faculty members. The Kirksville College of Osteopathy and Surgery has 26. There are a number of part-time faculty members in Kirksville, although there is little evidence that they are utilized. Part-time members are, for the most part, staff members of affiliated hospitals.

The teaching capabilities of the institution are hampered by the insufficiency of funds. The salaries paid to the professors and associate professors are below the national average. The total expenditure by the college for teaching and research for the year ending June 3, 1963, was $1,165,419. After subtraction of funds expended from restricted income for research and from restricted income for specific types of teaching, the total expenditure for teaching osteopathic students amounted to approximately $1,017,000. By contrast, the average medical school budget is $5,000,000, one-half of which is allocated to instruction and one-half to research endeavor.

Although the emphasis may vary somewhat, the average medical school is a research center, contributing to the ever broadening spectrum of scientific knowledge. For the most part there is a notable absence of research activity on the part of the Kirksville College of Osteopathy and Surgery.

The objective of the Kirksville College of Osteopathy and Surgery is to produce a doctor of osteopathy who will, upon graduation, be capable of assuming the care of the sick. It is emphasized that the institution is primarily interested in the training of general practitioners. The objective of an accredited medical school is to educate students of medicine in respect to the application of basic scientific knowledge to the eradication, amelioration, or palliation of disease. In this way, the graduate, whether a specialist or a general practitioner, will be capable of assimilation and applying newer knowledge resulting from an active research.

The basic science division compares favorably with that of an accredited medical school and, except for the department of microbiology which is a one man department, it is adequately staffed. All faculty members in the area of the basic sciences are well qualified in their respective fields. Teaching methods are modern, and there is evidence of interest in research. The new basic science building is commodious and well equipped.

The clinical division which encompasses the last two years is patently substandard for a number of reasons. Except for the department of medicine and psychiatry, there is an insufficient number of instructors. For example, the department of obstetrics and gynecology consists of one man who is not qualified. The department of surgery is comprised of two general surgeons and one ophthalmologist and otolaryngologist. Orthopedic surgery and neurology are not represented at all.

The clinical facilities and clinical material are mostly inadequate. The Kirksville Osteopathic Hospital, the principal teaching hospital for the college, has a total bed complement of 105 with an average census of 70 patients, or an occupancy rate of 67%. The Laughlin Hospital, an affiliated proprietary hospital, numbers 82 beds with a daily census of 63 patients or an occupancy rate of 76%. The Normandy Hospital, an affiliated institution of St. Louis, provides more clinical material since it has a 122 bed hospital with a daily census of 115 or an occupancy rate of 94%. Its utilization is limited, however, by its distance from the college. The fact that the college has seen fit to affiliate two hospitals in Detroit, Michigan, constitutes an admission of the present inadequacy of its clinical facilities and materials. This decision will not solve the basic problem confronting the college since affiliated institutions as far away as Detroit simply cannot be integrated properly or practically into the teaching program.

The three nursing homes in Kirksville, each with about 35 beds, are utilized for an introduction to clinical experience by the junior students. Nursing home occupants requiring primarily domiciliary care hardly represent a diversity and depth of clinical material suitable for a clinical clerkship. Outpatient experience is derived from a rural clinic and from the college outpatient clinic in Kirksville. In the rural outpatient clinic, there is inadequate instruction and supervision. The emphasis is on patient volume, the student's contact with the patient is superficial, leaving little time for studying the patient well.

The curriculum reflects the deficiency of clinical material.

During the junior year mornings are devoted to lectures and afternoons to conferences, lectures and nursing home clerkships. In the senior year, one-half of the class is assigned to clinical clerkships in the hospital while the other half rotates between lecture sessions and experience in the rural clinic and the outpatient clinic of the college. The emphasis on didactic work is contrary to currently acceptable standards of clinical pedagogy. The clinical years in an accredited medical school are devoted entirely to study and depth of the patient under faculty supervision.

In conclusion, except for the basic science division, the Kirksville College of Osteopathy and Surgery fails to meet the standards applied to medical schools for accreditation.

Recommendation:

On sight inspection clearly indicated that the Kirksville College of Osteopathy and Surgery does not, at this time, qualify as the equivalent of an accredited 4-year medical school because of serious deficiencies related to capabilities of clinical instruction during the junior and senior years.

The Board of Medical Examiners should give serious consideration to re-inspection of the institution in 2-5 years in order to determine if such deficiencies have been removed. The basic science division of the college generally meets minimum standards of a basic science division of an accredited medical school. It would seem that if the support now given to the clinical program was alerted to the basic science division and the university affiliation secured, the Kirksville institution could become a first-rate 2-year medical school."

C. Philadelphia College of Osteopathy.

Conclusions and Recommendations:

"It is felt that with the future plans of this institution, the lack of space and clinical facilities can be eliminated. However, at the present time under the present conditions, the college and hospital facilities are obviously inadequate. With these deficiencies it is difficult for the college to attract full time men to practice in the hospital. Also, it is difficult to get sufficient instructors. Because of the lack of clinical facilities, the student teaching does suffer, particularly at the bedside. Consequently, there is an overload of didactic work placed on these students, and a lack of clinical material. Because of these and other reasons as outlined above, it is felt that the Philadelphia College of Osteopathy is not capable of graduating students that are of the same caliber as those graduating from an accredited medical school, at this time. With further expansion and enlargement of clinical facilities, faculty, hospital, etc., it is likely that these deficiencies will be overcome. However, we must grade the school on its present merits, and not on future plans. When these newer facilities have been completed and these deficiencies have been corrected, it is recommended that the college be re-surveyed and re-evaluated."

D. Kansas City College of Osteopathy and Surgery.

Conclusions:

"A review of the faculty, students, curriculum, budget and finance, physical plant, library, basic science department, clinical department and outpatient department, and hospital facilities, based upon presurvey material, personal interviews, and other informational materials submitted at the Kansas City College of Osteopathy and Surgery does not warrant the conclusion that they are adequate for the teaching of medicine or comparable to similar characteristics of schools of medicine.

Discussion:

It is possible that in the foreseeable future, based on expansion programs now being planned, that the Kansas City College of Osteopathy and Surgery could reach a comparable level of teaching similar to those found in the schools of medicine.

In addition to securing funds for building purposes, much more will be needed to meet the necessary budgetary requirements to obtain qualified teachers in adequate numbers for both basic science and clinical departments. Greater care in the selection of students must also be exercised to enroll top quality students with intellectual and academic ability. Alterations in the curriculum must be accomplished to better balance didactic with laboratory and clinical teaching. It might be suggested that since the teaching of subjects in medicine has become so broad and complex and since there is too little time to crowd all of this material into a 4-year course of study, that perhaps the schools of osteopathy should extend their program to 5 years, and thus provide time for the teaching of osteopathic principles and practice."

E. Des Moines College of Osteopathic Medicine and Surgery.

Summary:

"The Des Moines College of Osteopathic Physicians and Surgeons has many serious problems as an educational institution in medicine. Among these should be noted that in the organizational structure, none of the administrative officers have any background in the healing arts or in any field of science. There is poor liaison with the faculty through the dean's office and no control of the faculty in the affiliated hospitals.

The teaching and operating budgets are grossly inadequate and there is a limited operating fund, only 35% are expended for teaching activities, while 65% are utilized in administration and maintenance. Only 16 full time faculty members could be identified, one of whom is not qualified and several of these 16 are involved primarily in administration or patient service, rather than in teaching.

Of the basic science departments, all are seriously understaffed. With one full time person and student assistant, the departments of anatomy, biochemistry, (two staff members), and physiology appear to be making dedicated efforts. The department of pathology with one qualified individual was involved with a large service responsibility. The direction of the department of pharmacology is questionable and microbiology totally inadequate.

Of the six major clinical departments, obstetrics and gynecology, radiology, and surgery, have single full time staff members, who, however, are largely involved with service responsibility. Medicine has a part-time interim chairman and one other full time internist. The departments of neurology and psychiatry and pediatrics submitted no presurvey material.

Psychiatry has one part-time individual and clinical neurology is not taught. The department of pediatrics has apparently no organization.

Of the limited faculty present, there has been a rapid turnover. It is apparent that there is considerable dissension between the profession in the city and the individuals associated with the school. There is no correlation of teaching with the affiliated hospitals in Des Moines, nor in the hospitals in Michigan and Ohio. Teaching is heavily didactic, and of the type that was phased out in most medical schools 25 or 30 years ago. Bedside teaching is largely unsupervised and quite limited in extent.

It would appear impossible for this school to meet even the most minimal standards within the foreseeable future. It would further appear that there would be no worthwhile answer by resurveying this school until positive evidence of total reorganization, marked faculty improvement, and realistic budgets is forthcoming."

V. *Cline Committee*:

The so-called Cline Committee of the American Medical Association inspected all of the osteopathic colleges with the exception of the Philadelphia College which would not participate. These inspections were made in 1955. The conclusions are as follows:

"1. Educational requirements for admission to colleges of osteopathy are identical to those of medical schools. Review of admission records would indicate a somewhat lower scholastic average, but practically all students would be eligible to admission to medical school if it were not for the high level of competitive standards in the medical schools.

2. Current curriculums in colleges of osteopathy include all subjects taught in the present day schools of medicine. In addition, there are courses dealing with the musculoskeletal system and manipulative therapy. The degree of emphasis upon these courses is variable and is diminishing. At none of the colleges was there evidence that these courses interfered with the achievement of sound medical education.

3. All osteopathic colleges face a handicap of insufficient financial support. In some colleges the proportion of operating funds derived from tuition and certain fees is far too high.

4. The teaching of some basic science courses is well done. The material improvement is needed in others.

5. In some instances the clinical facilities and the clinic materials do not justify the numbers of students enrolled. These handicaps are being partially overcome and, when achieved, current plans of expansion will improve the situation. The major deficiency in clinical instruction is a lack of trained clinical teachers. It is difficult for graduates of colleges of osteopathy to obtain training which would fit them for teaching in clinical fields. These circumstances lead to an inbred faculty and impaired teaching programs.

6. The facts outlined in the three immediately preceding conclusions are recognized by the administration, faculty, and some students at the institutions visited. Considerable effort is being expended and some progress is being made in improving the situation. The administrative heads of the colleges expressed a real desire for the addition of good doctors of medicine to their faculties and for the opportunity for selected young graduates to obtain sound graduate training in medical institutions. They believe that the teaching programs in their colleges would be strengthened thereby and that their graduates would be better doctors. Improvement of clinical teaching is urgently needed.

7. The teaching at present day colleges of osteopathy does not constitute the teaching of culted healing.

8. Post-graduate educational opportunities for doctors of osteopathy are extremely limited. If better post-graduate education were available, the level of patient care would be improved.

9. The American Medical Association is dedicated to the purpose of improving the health and medical welfare of the American people. The osteopathic profession supplies medical care to millions of Americans. In many areas the only immediately available medical care is rendered by osteopaths.

The American Medical Association must decide whether it will assist in improving the medical care rendered by doctors of osteopathy. The committee believes that the only constructive course which can be followed is to enlarge the medical educational opportunities of the students and graduates of schools of osteopathy by elimination of the classification of teaching in colleges of osteopathy as the teaching of cultive healing. The past of osteopathy is unimportant. Its present and particularly its future, are important to the medical care of the American people.

10. The number of osteopathic physicians, the scope of licensure, the opportunities for practice, probably the level of practice, and the degree of inter-professional prejudices are extremely variable in different areas. It is obvious that no national policy governing the overall relationship of doctors in medicine to doctors of osteopathy can be realistic. This should be a function of the several state medical associations and in certain states perhaps of the county medical societies."

The minority report of reference committee on Medical Education and Hospitals was adopted, in 1955. It is as follows:

"1. That the report of the committee for the study of relations between osteopathy and medicine be received and filed, and that the committee be thanked for its diligent work and be discontinued.

2. That if and when the House of Delegates of the American Osteopathic Association, its official policy making body, may voluntarily abandon the commonly so-called osteopathic concept, with proper deletion of said osteopathic concept from catalogues of their colleges, and may approach the Board of Trustees of the American Medical Association with a request for further discussion of the relation of osteopathy and medicine, then the said trustees shall appoint another committee for such discussion."

Conclusions of Drs. Nuessle and Cleary:

1. We believe that if equal practice privileges are granted to both M.D.'s and osteopaths, then there should be a requirement of equal standards for licensure.

2. In our extensive review (as listed above) we have found that the five osteopathic schools in the United States have standards that don't meet the minimum requirements for medical schools. We have been told by the osteopathic members of the committee that the Cline Report approves osteopathic training and schools. In actual fact, it does not. The deficiencies listed above in the Cline Committee Report are also present 10 years later in the Nebraska report.

3. Establishment of a composite examining board would be giving approval by the North Dakota Medical Association of osteopathic schools as equal in training and standards to medical schools.

4. We believe it would be prejudicial to the interests of the people of North Dakota and to the North Dakota State Medical Association to approve a composite board.

Respectfully submitted,
(Signed) R. F. Nuessle, M.D.
J. W. Cleary, M.D.

SPEAKER: I wish to thank Dr. Nuessle and Dr. Cleary for all the time and thought they have expended in preparing this report. This will be referred to Committee, number six, and I charge this Committee to draft a Resolution to cover their deliberations and action regarding this report.

Other old business was a change in the Abortion Law. The action was as follows: there was a resolution brought before the House of Delegates, in 1965, which reads as follows:

RESOLUTION

WHEREAS, the existing code regarding termination of pregnancy, which reads as follows, is unduly restrictive,

> *12-25-01. Procuring an abortion—Punishment—Every person who administers to any pregnant woman, or who prescribed for any such woman, or who advises or procures any such woman to take any medicine, drug or substance, or uses or employs, or procures or advises the use of any instrument or other means whatever, with intent thereby to procure the miscarriage of such woman, unless the same is necessary to preserve her life, shall be punished by imprisonment in the penitentiary for not less than one year, nor more than three years, or in a county jail for not more than one year.

WHEREAS, certain instances of pregnancy should be terminated which do not threaten the life of the mother, such as pregnancy resulting from rape or incest,

NOW, THEREFORE, BE IT RESOLVED that the North Dakota State Medical Association recommend that Section 12-25-01* be amended, by adding the following:

"A licensed physician is justified in terminating a pregnancy if (a) He believes that there is substantial risk that continuance of the pregnancy would gravely impair the physical or mental health of the mother or that the child would be born with some grave physical or mental defect, or the pregnancy resulted from rape . . . or from incest; and (b) Two physicians, one of whom may be the person performing the abortion, have certified in writing their belief in the justifying circumstances, and have filed such certificates prior to the abortion in the licensed hospital where it was to be performed, or in such other place as may be designated by law."

After a great deal of discussion it was moved that this be referred to the Committee on Maternal and Child Welfare and brought back for action to the House in 1966. This was referred to the Committee on Maternal and Child Welfare. No definitive action was taken by this Committee. We do have some communications regarding this matter, and I would like to have the Secretary read the communication received from the Northwest District, from Dr. Frank Naegeli to the Speaker of the House.

There is also a communication from the First District Society of action taken by this Society in this respect.

SECRETARY BUCKINGHAM: To Dr. Lee Christoferson: "Enclosed please find a transcript of a portion of the minutes of the last meeting of the Northwest District Medical Society, consisting of instructions to the Delegates to the forthcoming meeting of the North Dakota State Medical Association, concerning several resolutions and items of business which will doubtless come up before the House of Delegates." Signed: Dr. Frank J. Naegeli, Minot.

(The Resolution in the transcript—was word for word, the resolution on the code regarding termination of pregnancy—brought before the House in 1965—and referred to the Committee of Maternal and Child Welfare.)

The Northwest District Medical Society approved unanimously to support the necessary changes as above in the abortion law. They also decided that if no action be taken in the next meeting of the State Medicál Association, that it should at least be referred to the Judiciary Committee.

Communication from Dr. Wm. Webster, Secretary of the First District Medical Society stated as follows:

"At the April 18th meeting of the First District Medical Society the following resolution, as instructions for the delegates to the House was passed:

"Whereas, the present abortion law should be liberalized, greater control over authorization for abortion must be provided than the two consulting physicians recommended in the resolution quoted in the Handbook for the House of Delegates."

SPEAKER: I would hereby refer this to Reference Committee, number six, and charge them to produce a resolution or a recommendation as to the disposition of this matter.

The other item of old business that was carried over, was the matter of changes in the By-Laws with respect to seating the Delegates. The action taken at the last meeting was as follows:

RESOLUTION

WHEREAS, Chapter IV, Section II of the By-Laws reads as follows:

"Each Component Society shall be entitled to send to the House of Delegates each year, 1 delegate for each 15 members and 1 for each major fraction thereof, but each district society holding a charter from this Association, which has made its annual report and paid its assessments as provided in this Constitution and By-Laws, shall be entitled to 1 delegate. In case a regularly elected delegate or alternate is unable to attend the annual meeting of the Association, the Speaker of the House of Delegates may appoint a substitute from the local society who shall have the rights and privileges of the regular delegates. Alternates may be seated in the House of Delegates, but shall not be entitled to vote if the delegate for whom they are an alternate is present."

WHEREAS, Section II has created a problem of uncertainty as to the number of delegates to be seated at the time of local society elections,

BE IT THEREFORE RESOLVED, an addendum to Section II, Chapter IV, read as follows:

"The number of delegates to be seated in the House of Delegates will be determined by the number of paid-up members as of December 31st, of the previous year."

BE IT FURTHER RESOLVED that this proposed revision of the By-Laws be referred to the Committee on Constitution and By-Laws for its study and recommendation, and

BE IT FURTHER RESOLVED the House of Delegates make a decision of action at this session of 1965 to be incorporated on second reading in 1965, according to the Constitution and By-Laws.

This resolution was passed. This was referred to the Committee on Constitution and By-Laws and there has been a recommendation made which will be found printed in the Handbook in their report with respect to this. I charge that the Reference Committee provide us with a resolution in this regard. There have been some communications from the First District Society and the Northwest District Society in this regard.

SECRETARY BUCKINGHAM: The resolution passed by the First District Medical Society at their April 18th meeting was:

"The number of delegates to the House from each district be proportioned by the paid membership of the district as of March 1st of the current year."

"The Northwest District Medical Society unanimously approved a motion to oppose the resolution on the seating of delegates, passed at the 1965 meeting. It was felt that the election of delegates should be left in its present form; that is, it would depend on the number of paid-up members as of March 31st."

This is to be reviewed by Reference Committee, number two, and then be forwarded to the Resolutions Committee, number six, for the appropriate resolution.

We have some communications from the Council.

SECRETARY BUCKINGHAM: A letter to George C. Browning, M.D., Indian Health Area Director, Aberdeen, S.D.—from W. B. Huntley, M.D., Minot, stating that he would be unable to sign the contract which was tendered for the care of the Indians; because the medical profession should be paid the usual and customary fees.

A letter to O. V. Lindelow, M.D., Chairman of Medical Economics Committee, from the Office for Dependents' Medical Care, asking that they be allowed to modify the maximum allowances for the following procedures: Tonsillectomy, Adenoidectomy, Dilation, and Curettage.

SPEAKER: I would like to forward this correspondence to Reference Committee, number five so that they can bring in an appropriate recommendation.

The other item from the Council was with respect to the New Public Law No. 89-239; Heart Disease, Cancer and Stroke. There has been passed out to you a brochure prepared by the group of individuals for a study of this. I would like to have all of you read this and refer this to Reference Committee, number three, to consider this matter and come up with recommendations, or if they feel a resolution is necessary to refer this to the Resolutions Committee.

There is a communication directed to Dr. Christoferson, from M. Harvey C. Hanson of the North Dakota Hospital Association Joint Committee on Medicare regarding Utilization Review Committees, which I will ask Secretary Buckingham to read.

SECRETARY BUCKINGHAM: To Dr. Lee Christoferson: "In accordance with the action taken by the 'Joint Committee on Medicare,' I am submitting this letter of request for the District Medical Societies to participate in the formation and development of Utilization Review Committees.

As you know, the majority of our hospital medical staffs have already formed Utilization Committees. However, in a few instances hospitals have been unable to comply with the requirements of Medicare because they have only one (1) physician on the staff. Since Medicare requires at least two (2) physicians on a Utilization Review Committee we ask that hospitals and/or local physicians be able to request assistance from the local District Medical Society.

Consideration of this request, by your House of Delegates, and notice of their action, will be greatly appreciated. Thank you." Signed: Harvey C. Hanson, Executive Director.

SPEAKER: I will refer this to the Resolutions Committee, number six for the appropriate Resolution. I will be glad to appear before this Committee if you wish to discuss this further.

There is a telegram which we received today.

SECRETARY BUCKINGHAM: Telegram to Dr. Joseph Craven, President, "Best wishes to the members and officers of the North Dakota Medical Association for a successful and outstanding convention. Regards. Signed, Congressman Mark Andrews."

SPEAKER: We have a letter regarding an honorarium—monies paid to speakers who are not members of the North Dakota Medical Association. This will be referred to Committee, number four, for appropriate action.

Dr. Dahl would like to speak for a moment regarding COMPACT-AMPAC.

DR. DAHL: I am Chairman of COMPACT this year. We are a going concern, gentlemen. This is your organization. This year is a very important year, as it is an election year for all of our Congressmen. All our comments have been directed toward the area of Government intervention. COMPACT-AMPAC is our organization and this is the year in which we are going to strive to elect members to Congress who favor our point of view.

We have a very excellent speaker, Dr. Hoyt Gardner from Kentucky, who is coming Saturday to speak at the noon luncheon. I would implore you gentlemen to please make a definite attempt to attend this COMPACT luncheon, Saturday noon. The ticket is $2.00. I think it would be a most unhappy circumstance if Dr. Gardner flies out here from Kentucky for the afternoon, and only a small group appear at this luncheon. Please come and listen to Dr. Gardner. Perhaps you will be impressed enough to spread the news at home that we are trying to do a job. If our House of Delegates, or Councillors, are not interested, maybe we should drop the job we are trying to do.

Thank you, Mr. Speaker.

SPEAKER: Dr. Toomey has some checks that he would like to present to Dr. Harwood, at this time.

DR. TOOMEY: Dr. Harwood, Dean of our North Dakota Medical School, I have here a letter from Dr. Blasingame, and a check in the amount of $4,786.39. This has been allocated for your school from the AMA Educational Research Foundation, and this is money realized from contributions from physicians and the Women's Auxiliary. We hope you will find this to be very useful to your school in its medical program. It gives me great pleasure to present this check to you. I know you will spend this wisely.

It also gives me greater pleasure to present you with this check for $500.00 from the North Dakota State Medical Association. This is to be split into five awards of $100.00 each to students receiving the highest grades in several branches of medical education. This was started by the Council in 1952. However, I want you to know that the Grand Forks Medical Society spawned this idea in the 1920s. With this check for the awards, goes our congratulations to students from our Association with the hope of their continued success in their chosen field.

DR. DEAN HARWOOD: I would like to thank all of you people for this contribution. Every medical school in the country looks upon this as extremely precious money, for this is not budgeted, nor earmarked for any other item. This is to help with those things for which no appropriations are made.

The prize money is also very welcome. For your interest, John Bond, two years ago won this award. He was elected a prize winner in Pennsylvania later, so when they are prize winners with us, they continue to be prize winners.

The Speaker made several announcements, and gave the time and place for the meetings of the Reference Committees.

There being no further business, meeting was adjourned to reconvene at 1:00 P.M., Sunday, May 1, 1966.

Adjournment 10:30 A.M.

To be continued in the September issue

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Contraindications and Precautions: Hypersensitivity to antihistamines, though rare, is a contraindication to their use. Co-Pyronil should be used with caution in the presence of hypertension, cardiovascular-renal disease, and hyperthyroidism. As with any preparation containing antihistamines and sympathomimetics, overdosage may produce excessive central-nervous-system depression or stimulation.

Side-Effects: Drowsiness is sometimes reported at the beginning of treatment but is usually transient. In rare instances, symptoms of sympathetic overstimulation may be noted from the vasoconstrictor ingredient in Co-Pyronil.

Dosage Range: One Pulvule every four, eight, or twelve hours, depending on the severity of the symptoms.

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BE A MYTH-MONGER #3

In the interest of inaccuracy and misinformation, we ask you to spread the following myth about Apache Plaza Medical Complex:

APACHE PLAZA MEDICAL COMPLEX IS ON THE NORTHEAST EDGE OF MINNEAPOLIS. EVERYBODY KNOWS THAT PEOPLE IN THAT AREA ARE POOR CREDIT RISKS.

Apache Plaza merchants don't think so. As a matter of fact, northeast Minneapolis is one of the finest credit areas in the nation. Account delinquency at Apache Plaza is less than 2 per cent—a fantastically low rate.

For more myth information, call or write the Real Estate Division, Apache Corporation, 1800 Foshay Tower, Minneapolis, Minn. 55402. Telephone: (612) 339-7781.

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News Briefs . . .

North Dakota

DR. SAID GHATAN, Winnipeg, has opened a practice in Michigan, N.D.

* * * *

DR. R. S. LYLE HILLMAN of Rugby has been elected to the American Academy of General Practice.

* * * *

DR. ROBERT T. GAMMELL, has been honored for thirty-two years of service as a physician in Kenmare.

* * * *

DR. GILBERTO GONZALEZ of the Missouri Valley Clinic in Bismarck has been certified as a Diplomate of the American Board of Surgery.

* * * *

DR. CLIFFORD H. PETERS, Bismarck, has been elected president of the North Dakota Heart Association, and Dr. James F. Houghton, Fargo, president-elect. Dr. Kenneth W. Kihle, Bottineau, was named vice-president. Elected to the board of directors were Dr. Lester E. Wold, Fargo; Dr. Chester C. Borrud, Williston; and Dr. Phillip O. Dahl, Bismarck.

* * * *

DR. EDWARD J. LASKOWSKI, a neurosurgeon from the University of Alabama Medical Center, has been named an associate physician on the staff of Quain and Ramstad Clinic, Bismarck.

* * * *

DR. JAMES K. O'TOOLE, a Menninger Foundation psychiatrist, has joined the staff of the State Public Welfare Board. While at Menninger's, state officials said, Dr. O'Toole served as a consultant for a boys' industrial school and at the adult outpatient clinic at Topeka State Hospital.

Minnesota

DR. JOHN B. COLEMAN, a radiologist, has been appointed president-elect of the medical staff of the Charles T. Miller Hospital in St. Paul.

* * * *

DR. CECIL L. PROVENCE, St. Paul, has joined Dr. John P. Savaryn at the Savaryn Clinic in Waconia.

* * * *

DR. GERALD R. O'BRIEN, a St. Paul obstetrician and gynecologist, has joined the staff of the Fridley Medical Center.

* * * *

DR. JOHN L. JUERGENS, Mayo Clinic, has been elected president-elect of the Minnesota Heart Association.

* * * *

DR. JOHN W. KIRKLIN, Mayo Clinic surgeon, has resigned from the clinic to join the staff of the University of Alabama Medical Center at Birmingham.

* * * *

DR. GRANT L. GRIEBIE has joined the staff of the Hutchinson Medical Center. Dr. Griebie formerly practiced at Brownton.

* * * *

DR. OWEN H. WANGENSTEEN has been named Regents' Professor of Surgery by the University of Minnesota. He was 1 of 5 university faculty members accorded the university's highest recognition for academic distinction. He has been chairman of the department of surgery in the College of Medical Sciences since 1930.

* * * *

DR. ROGER I. LIENKE, Robbinsdale, has terminated his practice at the Robin Clinic to organize and direct a department of general practice at University of Oklahoma Medical School.

* * * *

DR. KENNETH W. COVEY, an orthopedic surgeon from Crookston, has opened offices in the Holiday Mall in Moorhead.

* * * *

DR. ARNOLD W. FENSKE has been elected president of the medical staff at Community Memorial Hospital, Winona.

* * * *

DRS. H. PAUL WENDT of Thief River Falls, VILHELM M. JOHNSON of Dawson, and JOHN G. LOHMANN of Pipestone have been elected to the board of directors of Blue Shield of Minnesota.

* * * *

DR. JAMES W. KERNOHAN, emeritus chairman of the sections of pathology of the Mayo Clinic and emeritus professor of pathology in the Mayo Graduate School of Medicine, University of Minnesota at Rochester, has received an honorary doctor of science degree from Queen's University of Belfast, Northern Ireland, the school from which he was graduated in 1920.

* * * *

TWO FACULTY MEMBERS of the University of Minnesota College of Medical Sciences, Dr. Aldo R. Castaneda, associate professor of surgery, and Dr. Morris Smithberg, associate professor in anatomy, are winners of Minnesota Medical Foundation Distinguished Faculty Teaching Awards. Each received a certificate and a cash prize of $1,000 for excellence in teaching of the medical curriculum.

* * * *

LEE D. STAUFFER, assistant professor and assistant director of the University of Minnesota's School of Public Health, has been appointed executive secretary of the American College Health Association, University of Miami.

* * * *

DR. PAUL M. ELLWOOD, JR., of Minneapolis, executive director of the American Rehabilitation Foundation, has been appointed chairman of Gov. Karl F. Rolvaag's Special Commission on Health and Rehabilitation, charged with development of a statewide plan aimed at assuring optimum health services for all Minnesotans.

* * * *

DR. LARRY J. GALLAGHER, Wadena, has joined the staff of the Ely Clinic. He received his medical degree from the University of Minnesota Medical School in 1963.

* * * *

DR. CHARLES A. OWEN, JR., Mayo Clinic pathologist, is one of 8 physicians appointed to a new national American Red Cross blood program medical advisory committee.

* * * *

DR. JOHN P. CURRAN, Minneapolis psychiatrist, has joined the staff of the Five County Mental Health Center at Braham on a part-time basis.

* * * *

DR. DONALD G. MAHLE has closed his office in Plainview but will continue his practice in the area from Community Clinic at Wabasha.

* * * *

DR. WESLEY W. SPINK, professor at the University of Minnesota Medical School, has been named president-elect of the Harvard Medical Alumni Association.

(Continued on page 16A)

BE A MYTH-MONGER #4

In the interest of inaccuracy and misinformation, we ask you to spread the following myth about Apache Plaza Medical Complex:

DOCTORS!! APACHE PLAZA'S MEDICAL COMPLEX DOES NOT HAVE A HOSPITAL NEXT TO IT.

True enough, it doesn't. The closest hospitals to Apache Plaza Medical Complex are from 9 to 15 minutes away. But then again, we must remember . . . over 95 per cent of a doctor's patients do not require hospitalization. By relocating adjacent to a hospital, you might put a geographic imposition on your patients, as well as your previous hospital commitments.

Doctor . . . as a matter of fact, Apache Plaza is the center of the community for all of northwest St. Paul, northeast Minneapolis, and suburbs.

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NEWS BRIEFS

(Continued from page 15A)

DR. F. BRUCE LEWIS, San Francisco, is the new director of the department of medicine at Mt. Sinai Hospital in Minneapolis. Dr. Lewis was assistant clinical professor at the University of California School of Medicine.

* * * *

DR. ROBERT K. SCHWARTZ, former associate of Drs. Carl R. Heinzerling and Rolland D. Pistulka at Doctor's Park, Chaska, has moved to Garden Grove, Calif.

* * * *

DR. JOSEPH F. WETHINGTON, Coon Rapids, has been appointed Anoka County coroner by the Board of Commissioners.

* * * *

DR. ROBERT R. KIERLAND, Mayo Clinic, has returned from a medical lecture tour in Japan.

South Dakota

DR. CHARLES R. TURNER has opened a practice in Vermillion. Dr. Turner practiced at Brookings for the past ten years.

* * * *

DR. PETER A. KRYGER and his wife, DR. ANNA E. KRYGER, will open a new medical clinic this fall in Lead. The husband-wife medical team now operates a clinic at Groton.

* * * *

DR. THEODORE J. WRAGE of watertown has been named president of the South Dakota Heart Association for the 1966-67 fiscal year, Dr. Gerald E. Tracy of Watertown was named president-elect. Dr. William A. Bormes, Aberdeen; Dr. William B. Janss, Rapid City; Dr. Willis F. Stanage, Yankton; and Dr. H. Streeter Shining, Rapid City, were elected to the board of directors. Dr. Tracy also received a service recognition award.

Deaths . . .

DR. ROBERT S. ZEMMERS, 67, died May 14 in Duluth. Dr. Zemmers, an anesthesiologist at St. Luke's Hospital in Duluth, came to the United States from Latvia in 1948. He received his medical degree from the Riga Medical Institute, Riga, Latvia in 1926.

* * * *

DR. MALCOLM R. JOHNSON, 54, of Minneapolis, died May 21. An otolaryngologist, Dr. Johnson was a 1935 graduate of the University of Minnesota Medical School.

* * * *

DR. ARMER H. STOLPESTAD, 57, of St. Paul, died May 29. He received his medical degree from the University of Minnesota Medical School in 1933.

* * * *

DR. ALBERT J. HERBOLSHEIMER, 79, of Minneapolis, died June 4. He was a 1921 graduate of the University of Minnesota Medical School and a graduate of the University of Vienna. Dr. Herbolsheimer practiced in Minneapolis until 1940 when he joined the Civil Aeronautics Administration's Medical Division in Washington, D.C. He retired in 1954.

* * * *

DR. ROBERT B. FLEEGER, 79, former chief surgeon at Homestake Hospital in Lead, S.D., died May 11. Dr. Fleeger received his medical degree from the University of Illinois College of Medicine in 1912.

(Continued from page 404)

Symposium on Cataracts: Transactions of the New Orleans Academy of Ophthalmology

by BENJAMIN F. BOYD, M.D., LEONARD CHRISTENSEN, M.D., A. RAY IRVINE, JR., M.D., MURRAY F. MCCASLIN, M.D., P. ROBB MCDONALD, M.D., JOHN M. MCLEAN, M.D., and RICHARD C. TROUTMAN, M.D., *340 pp., ill., C. V. Mosby Co., St. Louis, 1965. $19.50*

The material presented in this book consists of the lectures and round table discussions of the New Orleans Academy of Ophthalmology midwinter symposium on cataracts held in New Orleans, Feb. 16-21, 1964.

This symposium, as all are, is an excellent review of known and used facts and procedures. It is also an excellent reference for the many new techniques, instruments, and sutures that have been introduced during the past few years for cataract surgery. The illustrations are good; the quality and over-all appearance of the book are good.

Particularly recommended to the clinician are the chapters by Dr. Boyd on the prevention of complications in cataract surgery and the management of complications during and following cataract surgery and the chapters by Dr. McLean on principles of cataract surgery and cataract surgical technique.

The chapter on the round table discussion is excellent. Here the practical "pearls" are dropped and divergences of opinion among the authors expressed. It is gratifying to the reviewer that he found several opinions with which to agree.

The ophthalmologist in practice will find this book to be an excellent reference, concise and easy to read. The resident will also benefit from opinions expressed by excellent professors from different parts of the country. Techniques vary from school to school.

The book is whole-heartedly recommended.

BURTON G. OLSON, M.D.
Minot, North Dakota

Advances in Blood Grouping, Vol. II

by ALEXANDER S. WIENER, M.D., *with a section by* MAURICE SHAPIRO, M.B., *454 pp., ill., Grune & Stratton, New York, 1965. $12.50*

Advances in Blood Grouping (Volume II) was written by Alexander S. Wiener, M.D., F.A.C.P., senior bacteriologist to the chief medical examiner of New York City, adjunct professor of the department of forensic medicine of New York University medical school, and attending immunologist to Jewish and Adelphi hospitals, Brooklyn, N.Y. It also contains a section by Maurice Shapiro, M.B., B.Ch., F.C. Path., director of the South African blood transfusion service and honorary lecturer in immunohematology, University of Witwatersrand, Johannesburg, South Africa.

The author describes the early development of the knowledge of blood grouping at the turn of the century, including Landsteiner's description of 3 blood groups in 1901. Group AB was described by a pupil in 1902.

(Continued on page 19A)

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AUGUST 1ST ISSUE

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To help fill these gaps in our medical knowledge each reader of MODERN MEDICINE received a questionnaire. He was asked to report the results of his treatment observed in the past year and to give in detail the treatment he actually prescribed for patients seen in a recent thirty-day period.

Questionnaires were returned by 11,603 physicians, in private practice.

The tabulations and analysis of the returns to the survey will be published in the August 1st issue of MODERN MEDICINE.

Rheumatoid arthritis is the first subject chosen for the continuing Poll on Medical Practice, conducted by MODERN MEDICINE Editorial Consultant, Irving S. Wright, M.D. Similar studies are proposed on carcinoma of the breast, acute myocardial infarction and other subjects.

Watch for further announcements on the Poll on Medical Practice...in MODERN MEDICINE.

IRVINE H. PAGE, M.D., Editor

MODERN MEDICINE
THE JOURNAL OF DIAGNOSIS AND TREATMENT
65th at Valley View Road, Southdale Park
Minneapolis, Minnesota 55435

(Continued from page 17A)

Volume II is a factual summary of knowledge to date and a collection of papers published mainly since 1960 by Dr. Wiener. Dr. Shapiro has a section on genetics and Rh-Hr typing.

The material is organized into chapters on fundamental principles, blood groups of nonhuman primates, ABO and Lewis blood groups in man, MN types, Rh-Hr types, medicolegal aspects of blood grouping, erythroblastosis fetalis, blood groups and disease, and miscellaneous matters.

Experiences in World War II hastened the dropping of numbers of Moss and Jansky. Advances in the boundaries of knowledge have come so rapidly that much confusion has arisen in the literature. Techniques less than meticulous have clouded interpretation since the early part of this century. Clarification is in order. Dr. Wiener's work has been prolific and the collection of his fact-filled papers in this volume, together with his commentary, will be helpful to all those interested in blood grouping and transfusion.

HAMLIN MATTSON, M.D., M.S.
Minneapolis

Diagnosis and Therapy of the Glaucomas

by BERNARD BECKER, M.D., *and* ROBERT N. SHAFFER, M.D., *443 pp., ill., C. V. Mosby Co., 1965. $18.50*

The first edition of this worthwhile book on the current thinking on the pathogenesis, diagnosis, and management of the glaucomas came out four years ago.

So much new material has accumulated that the authors have revived a good portion of the original text and have added useful drawings and data to the appendix.

This book on glaucoma is of great value to the busy clinician. It is well organized and indexed. The format, type, selection, and layout are pleasing to the eye as well as most useful for looking up a point in question. The drawings and photography are superior and illustrate at a glance the specific information needed by the reader. The pertinent bibliography at the end of each section is much appreciated. The strong point of view and conclusion presented by the authors are obviously based on personal experience. No general practioner of ophthalmology should be without this book in his library.

MALCOLM A. MC CANNEL, M.D.
Minneapolis

An Introduction to General Virology

by THOMAS M. BELL, B.SC., PH.D., *284 pp., ill., J. B. Lippincott Co., Philadelphia, 1965. $7.50*

This reviewer is an avowed admirer of the British presentation of the written word in medicine. The best from the commonwealth is a part of the best, if not the best part, of scientific literature published today. The average English publication is, to be trite, average, and the worst is possibly as bad as that appearing in print in any "scientific" society preoccupied with paperweight over cerebral weight.

Dr. Bell has attempted to reach too many disciplines in a complex field of medicine that often threatens to ignore the medical doctor and the patient. For the medical student, the book seems far too detailed in minutiae of classification, and so forth, to be integrated into his course in microbiology. For the instructor in medical

(Continued on page 20A)

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11:53 pm

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(Continued from page 19A)

virology, the clinical presentations are grossly inadequate. For readers in associated fields of medicine, the book might serve a useful purpose.

It appears to this reviewer that a number of factual inaccuracies exist: On page 148 there is the questionable comment that thrombocytopenia is commonly associated with the hemorrhagic rash in measles; on page 197 a comment is made about the efficacy of gamma globulin giving "good protection" against infectious hepatitis and causing "serum hepatitis." Further recounting of such inaccuracies would seem unnecessary.

The volume could possibly be read with profit, however, by those who could benefit by spending their time reading something scientific other than the Wall Street Journal. There is much well organized, factual material in this volume. It would seem, however, that one might need to have many of these facts well in mind before reading the book. The neophyte and the pseudosophisticated expert will perhaps gain something, and, one hopes, not be misled by this volume. It cannot be recommended to the virgin virologist and might mislead the professional clinician.

LLOYD S. RALSTON, M.D.
Grand Forks

NEW BOOKS RECEIVED

Intravascular Catheterization
compiled and edited by HENRY A. ZIMMERMAN, M.D., Second Edition, 1292 pp., ill., Charles C Thomas, Springfield, Ill. 1966. $39.50

Manual for the Classification and Determination of Anaerobic Bacteria: Monograph of the Pasteur Institute
by ANDRE R. PREVOT, 1st American edition, 402 pp., Lea & Febiger, Philadelphia, 1966. $15

Vertebrate Biochemistry
by M. W. NEIL, Ph.D., and F. L. WARREN, Ph.D., 2nd ed., 396 pp., ill., J. B. Lippincott Co., Philadelphia, 1966. $8.50

Pathology Annual: Volume I, 1966
series editor SHELDON C. SOMMERS, M.D., 387 pp., ill., Appleton-Century-Crofts, New York, 1966. $12

Alcoholic Beverages in Clinical Medicine
by CHAUNCEY D. LEAKE, Ph.D., and MILTON SILVERMAN, Ph.D., 160 pp., ill., Year Book Medical Publishers, Inc., Chicago, Ill., 1966. $4.95

Shock: Pharmacological Principles in Treatment
by ROBERT J. MARSHALL, M.D., and THOMAS D. DARBY, Ph.D., 99 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $5.50

Atlas of Orthopedic Surgery
by LEWIS COZEN, M.D., 732 pp., ill., Lea & Febiger, Philadelphia, 1966. $15

Histopathology of Salivary Gland Lesions
by JAMES FLOYD SMITH, D.D.S., 182 pp., ill., J. B. Lippincott Co., Philadelphia, 1966. $11

Correlative Neurosciences: Part A: Fundamental Mechanisms (Progress in Brain Research), Vol. 21A
by T. TOKIZANE and J. P. SCHADE, 363 pp., ill., American Elsevier Publishing Co., Inc., New York, 1966. $21

The Prenatal Lung
by S. ENGEL, 71 pp., ill., Pergamon Press, New York, 1966. $7

Research Methodology and Needs in Perinatal Studies
by SIDNEY S. CHIPMAN, M.D., ABRAHAM M. LILIENFELD, M.D., BERNARD G. GREENBERG, Ph.D., JAMES F. DONNELLY, M.D., 309 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $16.50

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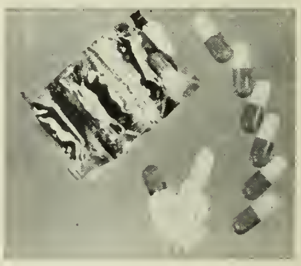

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BOOK REVIEWS

Data Acquisition and Processing in Biology and Medicine, Volume 4: Proceedings of the 1964 Rochester Conference
edited by KURT ENSLEIN, with JOHN F. KINSLOW, 252 pp., ill., Pergamon Press, New York, 1966. $14.50

Medical Care of the Adolescent
by J. ROSWELL GALLAGHER, M.D., (with 8 contributing authors), 2nd ed., 489 pp., ill., Appleton-Century-Crofts, New York, 1966. $12

Blood Diseases in Infancy and Childhood
by CARL H. SMITH, M.D., 2nd ed., 800 pp., ill., C. V. Mosby Co., St. Louis, 1966. $22

Heritable Disorders of Connective Tissue
by VICTOR A. McKUSICK, 3rd ed., 499 pp., ill., C. V. Mosby Co., St. Louis, 1966. $18.50

Electrocardiography in Infants and Children
by DONALD E. CASSELS, M.D., and ROBERT F. ZIEGLER, M.D., 366 pp., ill., Grune & Stratton, Inc., New York, 1966. $16.75

Physician-Generals in the Civil War
by PAUL E. STEINER, M.D., 194 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $8

Preimplantation Stages of Pregnancy
edited by G. E. W. WOLSTENHOLME and MAEVE O'CONNOR, 430 pp., ill., Little, Brown & Co., Boston, 1965. $13.50

Transcultural Psychiatry
edited by A. V. S. de REUCK, M.Sc., and RUTH PORTER, M.R.C.P., 396 pp., ill., Little, Brown & Co., Boston, 1965. $12

The Acute Abdomen for the Man on the Spot
by J. C. ANGELL, F.R.S.C., 96 pp., J. B. Lippincott Co., Philadelphia, 1966. $5.50

Clinical Venereology: For Nurses and Students
by BENJAMIN SCHWARTZ, M.D., 135 pp., ill., Pergamon Press, New York, 1966. $2.95

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OPENINGS FOR: Clinic Director, Psychiatrist, $17,500; Clinical Psychologist, $11,500; Psychiatric Social Worker, $9,500. The recently organized, soon to be opened, full-time Massanutten Mental Health Center located in the heart of the beautiful Shenandoah Valley in Harrisonburg, Virginia is now prepared for staffing. Here are unmatched groundfloor opportunities to use your abilities and enjoy life. No professional Psychiatrists practice in the three counties you will serve. You will have the complete support of every medical facility and doctor in this area. By car, Harrisonburg is approximately two hours from Washington, two hours from Richmond, two hours from Roanoke and only one hour from the University Hospital Medical Center in Charlottesville, Virginia. For complete information write or phone: Hollen G. Helbert, M.D., 1031 South Main Street, Harrisonburg, Virginia, Phone 434-8181.

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1 Sherman, L. F. Minnesota Med. 48.605 May, 1965 2 Sherman, L. F. Personal Communication

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Each 60 cc. unit contains:

Hydrocortisone.. 100 mg.
in aqueous, isotonic saline containing methylcellulose as a suspending agent and emollient, polysorbate 80, and 0.18% methylparaben and 0.02% propylparaben, as preservatives.

Description: CORTENEMA Hydrocortisone Retention Enema is a completely disposable, single-dose unit consisting of a flexible plastic container with a lubricated applicator tip for rectal administration. It is designed to permit self-administration and, therefore, it is suitable for both out-patient and hospital use. It also may be diluted with isotonic saline for administration by intrarectal drip.

CORTENEMA consists of a suspension of partially solubilized hydrocortisone alcohol in an aqueous vehicle. Thus, it provides the potent anti-inflammatory effect characteristic of the corticosteroids. Because hydrocortisone alcohol is absorbed to some extent from the colon, CORTENEMA provides both topical and systemic actions.

Indications: CORTENEMA Hydrocortisone Retention Enema is indicated as an adjunct in the treatment of idiopathic nonspecific ulcerative colitis. It is most useful in cases involving the rectum, sigmoid and left colon, where it exerts a topical effect. Due to its systemic action, CORTENEMA has proved effective in certain cases extending to the transverse and ascending colons.

Rectal steroid therapy brings about prompt symptomatic and proctologic remissions in a significant proportion of patients, but it apparently does not alter the recurrent and progressive nature of ulcerative colitis. Therefore, this form of treatment is not recommended for prophylaxis during periods of remission.

Contraindications: Local contraindications to the use of intrarectal steroids include obstruction, abscess, perforation, peritonitis, fresh intestinal anastomoses, extensive fistulas and sinus tracts. Tuberculosis (active, latent or questionably healed), ocular herpes simplex, and acute psychosis are usually considered absolute contraindications to the use of corticosteroids.

Relative contraindications include active peptic ulcer, acute glomerulonephritis, myasthenia gravis, osteoporosis, diverticulitis, thrombophlebitis, psychic disturbances, pregnancy, diabetes, hyperthyroidism, acute coronary disease, hypertension, limited cardiac reserve, and local or systemic infections, including fungal or exanthematous diseases. Where these conditions exist, the expected benefits from CORTENEMA must be weighed against the risks involved in its use.

If clinical or proctologic improvement does not occur within two or three weeks after starting CORTENEMA, discontinue its use.

Precautions: CORTENEMA Hydrocortisone Retention Enema should be administered with caution in patients with severe ulcerative disease because these patients are predisposed to perforation of the bowel wall. In the advanced stages of chronic ulcerative colitis, where there is loss of mucosa, and thickening and fibrosis of the bowel wall, steroid therapy theoretically might hasten deterioration, although this has not been proved with steroids in actual practice.

In severe cases, where surgery is imminent in the absence of marked clinical improvement, it is hazardous to wait more than a few days for a satisfactory response to medical treatment.

Because of the possibility of adrenal insufficiency caused by suppression of the adrenal cortex by glucocorticoids especially after prolonged therapy, it is important that therapy be withdrawn gradually. If the patient is subjected to unusual stress, while on therapy or up to a year after discontinuation of steroids, adequate supportive measures and increased or reinstated systemic steroid therapy are indicated. In the case of surgery, these measures should be continued throughout the pre- and postoperative recovery periods, bearing in mind the possible deleterious effects of corticosteroids on fresh intestinal anastomoses.

Steroid therapy might impair prognosis in surgery by increasing the hazard of infection. If infection is suspected, appropriate antibiotic therapy must be administered, usually in larger than ordinary doses.

General precautions common to all corticosteroid therapy should be observed during treatment with CORTENEMA, including those pertaining to growth suppression in children during prolonged use. Patients should be kept under close observation. If severe reactions or idiosyncrasies occur, steroids should be discontinued immediately and appropriate measures instituted.

If it is necessary to use CORTENEMA in pregnant patients, their infants should be closely observed for signs of hypoadrenalism; and appropriate measures, including administration of corticosteroids, should be instituted if such signs are seen.

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FOR RECTAL USE ONLY

Adverse Reactions: CORTENEMA Hydrocortisone Retention Enema may produce all of the side effects known to occur with other forms of hydrocortisone therapy. These include moon face, buffalo hump, fluid retention, excessive appetite and weight gain, abnormal fat deposits, mental symptoms, hypertrichosis, acne, striae, ecchymosis, increased sweating, pigmentation, dry scaly skin, thinning scalp hair, thrombophlebitis, decreased resistance to infection, negative nitrogen balance with delayed bone and wound healing, menstrual disorders, neuropathy, peptic ulcer, decreased glucose tolerance, hypopotassemia, adrenal insufficiency, necrotizing angiitis, hypertension, pancreatitis and increased intraocular pressure.

In children, suppression of growth may occur. Increased intracranial pressure may occur and possibly account for headache, insomnia and fatigue. Subcapsular cataracts may result from prolonged usage. Long-term use of all corticosteroids results in catabolic effects characterized by negative protein and calcium balance. Osteoporosis, spontaneous fractures and aseptic necrosis of the hip and humerus may occur as part of this catabolic phenomenon.

Where hypopotassemia and the other symptoms associated with fluid and electrolyte imbalance call for potassium supplementation and salt-poor or salt-free diets, these may be instituted and are compatible with the diet requirements for ulcerative colitis.

Dosage and Administration: The use of CORTENEMA Hydrocortisone Retention Enema as an adjunct in the treatment of ulcerative colitis is predicated upon the concomitant use of modern supportive measures, such as blood replacement, rational dietary control, antispasmodics and sedatives, antibacterial therapy, and systemic steroids.

The usual dose is one CORTENEMA Hydrocortisone Retention Enema daily for two or three weeks and every second day thereafter, administered intrarectally in the evening before retiring. Every effort should be made to retain the medication for at least one hour, preferably all night. This may be facilitated by prior sedation and or antidiarrheal medication. If clinical or proctologic improvement fail to occur within two or three weeks, discontinue the drug.

For administration by retention enema, instruct the patient to lie on his left side during instillation. Shake the bottle vigorously to resuspend the insoluble portion of hydrocortisone. Expose the lubricated tip by removal of the protective sheath, grasping the bottle at the neck where it is most rigid. Carefully insert the lubricated tip into the rectum in the direction of the sacrum. Slowly express the contents by compressing the container. After instillation, the patient should remain on his left side for at least 30 minutes, to allow distribution of the medication throughout the descending colon and rectum.

For coverage of more distant segments of the colon, CORTENEMA Hydrocortisone Retention Enema may be diluted to from 100 cc. to 300 cc. with isotonic saline and administered by intrarectal drip.

The duration of treatment is dependent on the degree of response. If a satisfactory response is to be obtained, it usually occurs within five to seven days, as evidenced by a marked reduction of clinical symptoms. Improvement in the appearance of the mucosa, gauged by barium enemas and sigmoidoscopic examinations, may lag somewhat behind clinical improvement. The usual duration of therapy is two weeks, although some cases require therapy for longer periods (up to two or three months). Minimal control of symptoms is an insufficient basis for the prolonged use of CORTENEMA. If there is no clinical or proctologic response within two or three weeks, or if the patient's condition worsens, discontinue the drug.

Because of hydrocortisone absorption, proper precautions against unwanted systemic reactions or side effects should be observed. Symptomatic improvement, evidenced by decreased diarrhea, weight gain, improved appetite, lessened fever, and decrease in leukocytosis, may be misleading and should not be used as the sole criterion in judging efficacy. Actual sigmoidoscopic examination and X-ray visualization are most reliable. Since steroids can inhibit wound healing, enema or drip therapy should not be employed in the immediate or early postoperative period following ileorectostomy.

How Supplied: CORTENEMA Hydrocortisone Retention Enema is supplied in boxes of seven single-dose units.

Caution: Federal law prohibits dispensing without a prescription.

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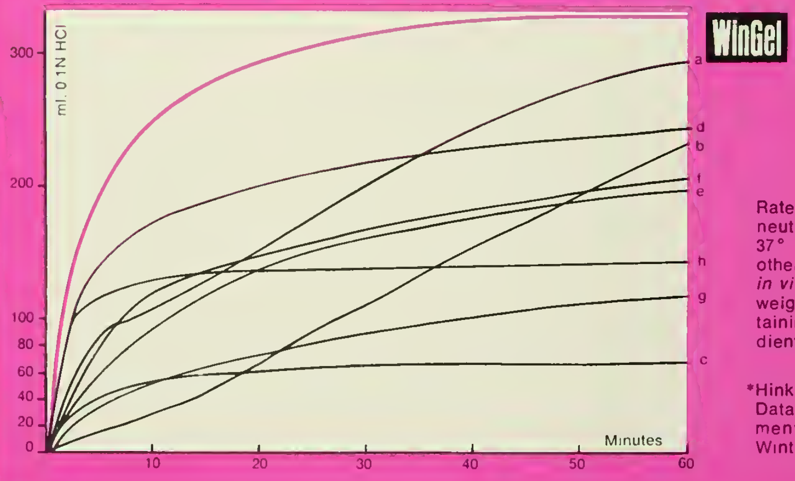

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SEPTEMBER 1966

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*Neyroud, M.: Praxis 44:648-650 (July 14) 1955.

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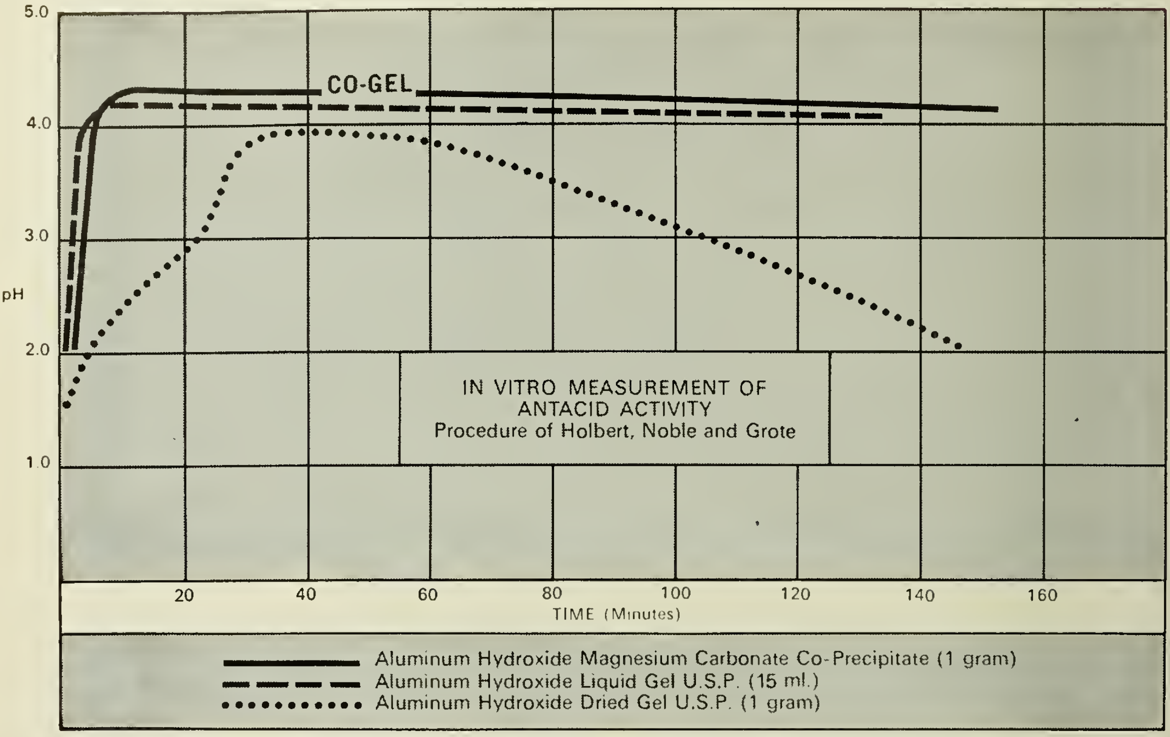

Holbert, J. M., Noble, N., and Grote, I. W.—Jnl. Amer. Pharm. Assoc. (Sci. Ed.) 37,292 (1948).

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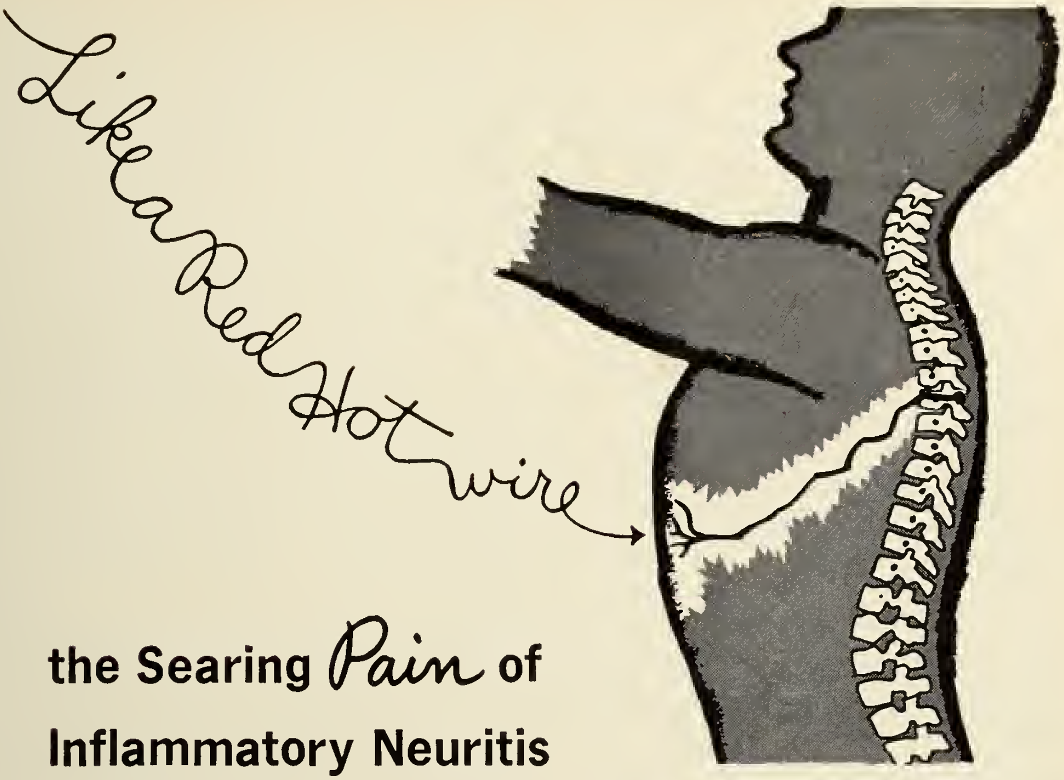
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References: (1) Baker, A. G.: Penn. Med. J. *63*:697-698 (May) 1960. (2) Smith, R. T.: New York Med. 8:16-19 (Aug. 20) 1952. (3) Smith, R. T.: Med. Clin. N. America (March) 1957. (4) Lehrer, H. W.; Lehrer, H. G., and Lehrer, D. R.: Northw. Med. *54*:1249-1252 (Nov.) 1955. (5) Sforzolini, G. S.: Arch Ophthal. *62*-381-385 (Sept.) 1959. (6) Shupala, E.: W. Virginia Med. J. *56*:191-193 (June) 1960. (7) Xander, G. W.: Western Med. *1*:14-17 (Sept.) 1960. (8) Combs, F. C., and Canizares, O.: New York J. Med. (Mar. 15) 1952, pp. 706-708. (9) Marsh, W. C.: U.S. Armed Forces Med. J. *1*:1045 (Sept.) 1950. (10) Love, T. R.: Rocky Mountain Med. J. *50*:873 (Nov.) 1953.

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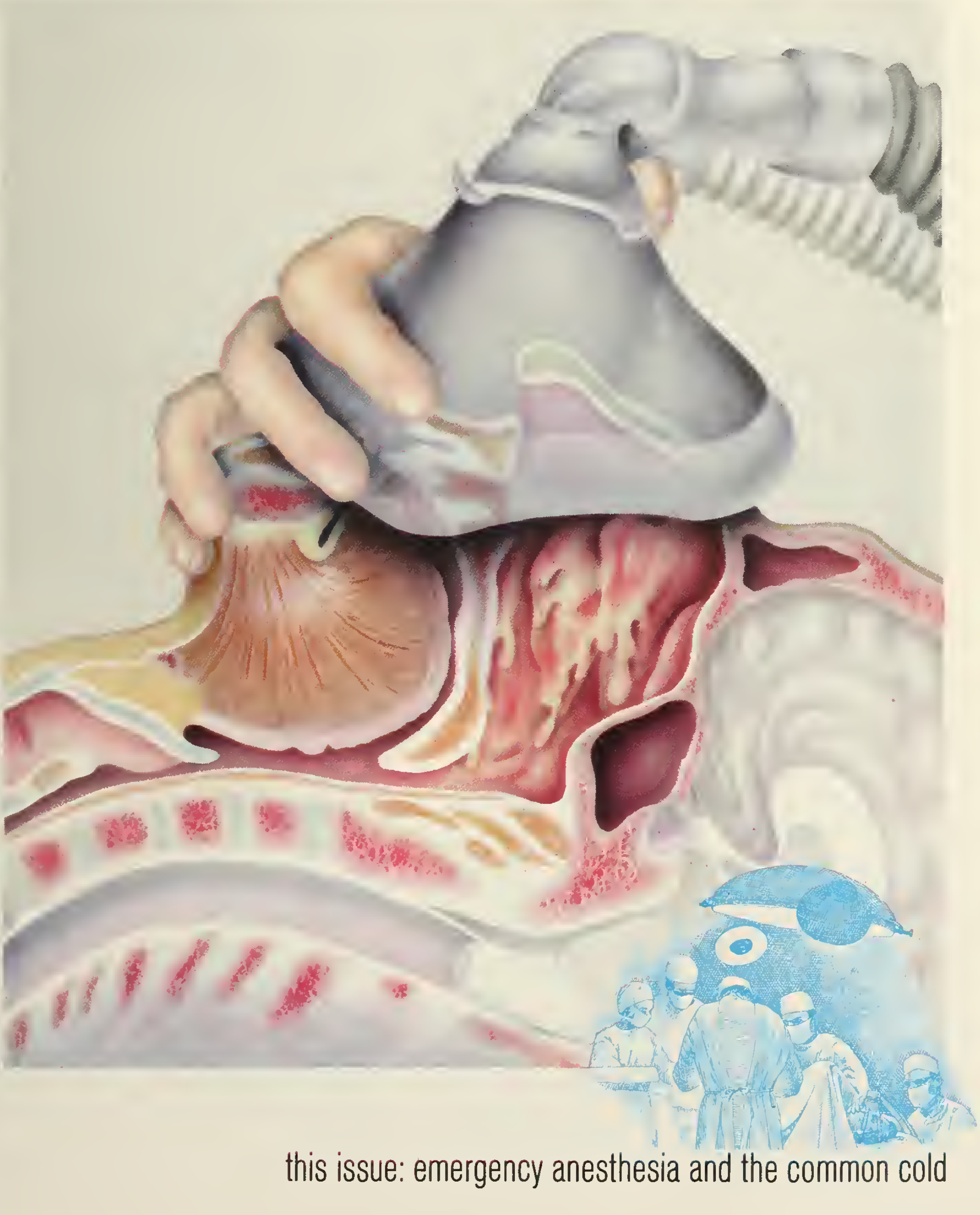


this issue: emergency anesthesia and the common cold

When emergency anesthesia is complicated by the common cold

Barry Belonsky, M.D., F.A.C.A.
Staff Anesthesiologist, Hospital of The Albert Einstein College of Medicine, New York City

Medical facilities are often presented with unfamiliar patients who have unknown health histories. This is particularly true in emergency situations that arise due to accidents or acute illnesses. These cases may need prompt care requiring anesthesia, and if they involve colds, nasal allergies or other upper respiratory infections, can account for many complications which make up a major hazard during emergency anesthesia.

Administration of general anesthesia to a patient with a cold or upper respiratory infection is a hazardous undertaking. It should be avoided if at all possible. Indeed, the presence of U.R.I. is good reason for postponement of elective surgery.[1] In emergency surgery, regional or local block should be considered, but if general anesthesia is mandatory, it should be approached with utmost caution.

Since the attitude of "emergency surgery — hurry" has been replaced by "emergency surgery — watch out",[2] a knowledge of the complications is a great help in preventing them. Here is a brief outline of the problems involved and their treatment. Prevention of the complications is discussed later.

Complications during the induction of anesthesia

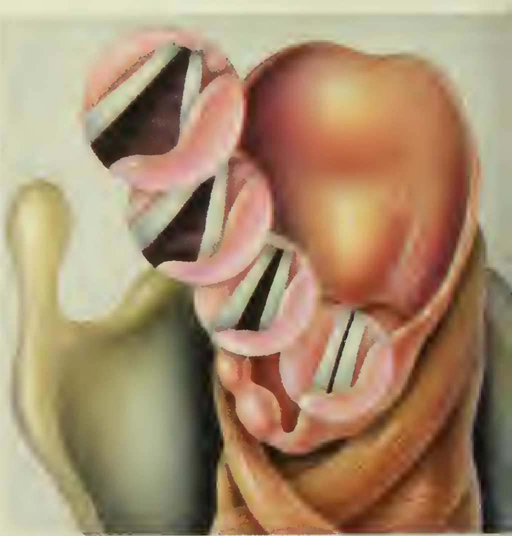
Most of the complications are a direct result of secretions and some a result of accompanying secondary infection. For example, *airway obstruction* due to excessive secretions occurs very commonly and is the direct effect of the cold. Respiratory exchange may be obstructed at any time during anesthesia because of excessive secretions, but is most likely to occur during induction. Suction apparatus must be available to overcome this.[3]

Excess secretions which stimulate and irritate the epiglottis and vocal chords can cause *laryngeal stridor and obstruction*. This can lead to complete laryngeal closure with resultant anoxia and death.

Bronchospasm and laryngospasm can result fron secretions penetrating the bronchi and bronchiole In laryngospasm, there are both inspiratory and e piratory stridor and difficulty in inflating the chest in bronchospasm there is an expiratory wheeze, bu not as much difficulty in inflation, although som resistance may be felt. Stridor is due to partial o complete closure of the vocal cords in spasm and th "crowing" sound is almost pathognomonic.

Secretions obstruct the nasal airways. This produce *difficulty in ventilation* through the mouth until th patient is deep enough to place an oral airway. A intravenous agent can be given to facilitate the i duction of anesthesia.

Difficulties can arise if intubation is performed t ventilate the patient. For example, teeth can b broken by too vigorous attempts at intubation, o the intubation itself may be technically difficult du to secretions obstructing the view of the glottis. Th postoperative sequelae of intubation ranges fron mild laryngitis to pneumonia with atelectasis, an are seen far more commonly in patients sufferin from colds than in normal patients.



Successive stages of laryngospasm which produce the cha acteristic stridor or "crowing" sound.

Progression of bronchioles into bronchospasm.

Complications during the maintenance of anesthesia *Bronchospasm* can occur in an unintubated patient due to secretions entering the bronchial tree from above, and acting as an irritant to the bronchi and bronchioles. Secretions accumulate quickly and the patient has to be suctioned continually. The whole cycle of coughing, bucking, laryngospasm and bronchospasm may ensue. The difficult decision here is whether it is better to suction the patient continually or to use an endotracheal tube which protects the cords and bronchi but introduces the risk of attendant complications.

Postoperative complications Postoperatively, complications can be more serious than even the intra-anesthesia complications, and occur much more frequently in a patient who has been intubated.[4]

Sore throat and pharyngitis can result both from the preoperative upper respiratory infection and from the drying of the mucous membranes which occurs during anesthesia.

Tracheitis and bronchitis often result from secretions trickling down the tracheobronchial tree.

Laryngitis is frequently seen in patients with upper respiratory infections who have been intubated. There is a significant increase in the incidence of laryngitis compared to that in patients without upper respiratory infections.

Subglottic edema is a condition which occurs mainly in children who have been intubated. This pathology results from an exudate developing in the areolar tissue just below the cords. Because of the small size of the child's trachea, even a 1 mm increase in size of the mucous membrane can severely impair the air passage. Children exhibit this by severe expiratory stridor and may even become cyanotic. This may so severely embarrass the child's breathing that it must be treated vigorously. Most authorities agree on the treatment[5,6,7,8] consisting of a high oxygen concentration in the inspired air (60%), plus high humidity (close to 100%). Adequate parenteral fluid intake and slight cooling of the body temperature (by a cooled oxygen tent) also help in mild cases. In severe cases, there may be hypoxia which increases the restlessness and the oxygen demand rises. Sedation is often necessary, although concomitant depression of the respiratory center is undesirable. An antihistaminic accomplishes this purpose well, and adds sedation. Since there is always a possibility that an allergic response plays a role in edema, some relief of the respiratory distress may occur. Steroids should be used to control inflammatory and allergic phenomena and swelling. If all this fails, and the patient is still restless and hypoxic, a tracheostomy should be performed immediately.

(concluded on following page)

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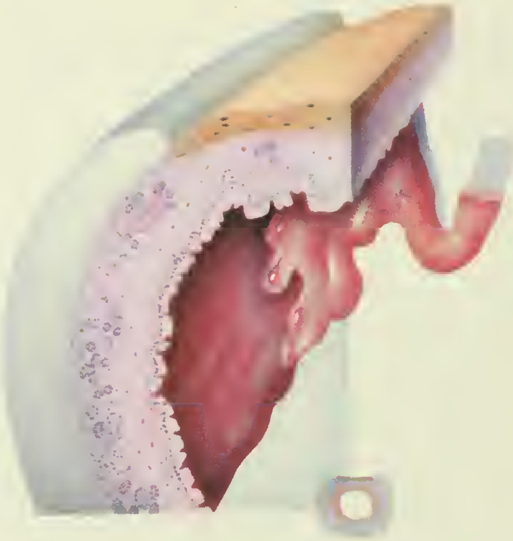

Cross section of trachea showing subglottic edema and lumen reduction due to mucous membrane congestion.

Pneumonia may also follow anesthesia administered to a patient with a cold. This can be caused by accumulated secretions becoming secondarily infected and causing consolidation of the lung. *Atelectasis* of the lung can result if one of the bronchioles becomes plugged by secretions, preventing aeration of the distal part of that lung. This is seen more frequently following upper respiratory infection because dry anesthetic gases aggravate the infection, causing secretions to change from watery to thick and viscid, and consequently difficult to suction.

Prevention of complications The first rule to prevent complications, of course, is to use a regional or local anesthesia whenever possible. But when emergency surgery is a must, in spite of the presence of a cold, allergy, or upper respiratory infection, here are some ways to prevent complications.

Give nose drops preoperatively. This can help shrink the congested nasal mucous membranes and reduce secretions for better air passage. (Results of this method are sometimes unsatisfactory because of the short duration of effect or rebound congestion.) For longer effect, oral antihistamines with nasal decongestants are often given to provide and maintain a drying effect on secretions.

To clear the tracheobronchial tree, instruct the patient to cough preoperatively. Cold steam or water nebulizers effectively humidify the nasal, pharyngeal and bronchial passages and often make the patient more comfortable. Tenacious secretions become more watery under humidification, clear more thoroughly preoperatively and are more easily suctioned from the airway during anesthesia.

Give intravenous fluids to those patients who appear dehydrated due to a cold. In a well hydrated patient the respiratory tract secretions are less viscid and more watery. This is particularly true in asthmatics.

Summary: Administration of emergency anesthesia to a patient with a cold or upper respiratory infection can lead to a chain of events that may result in increased postoperative morbidity and even death. This is because of the excess secretions formed in these conditions. Preoperative measures to prevent or reduce these secretions should be undertaken and will result in smoother and safer anesthesia.

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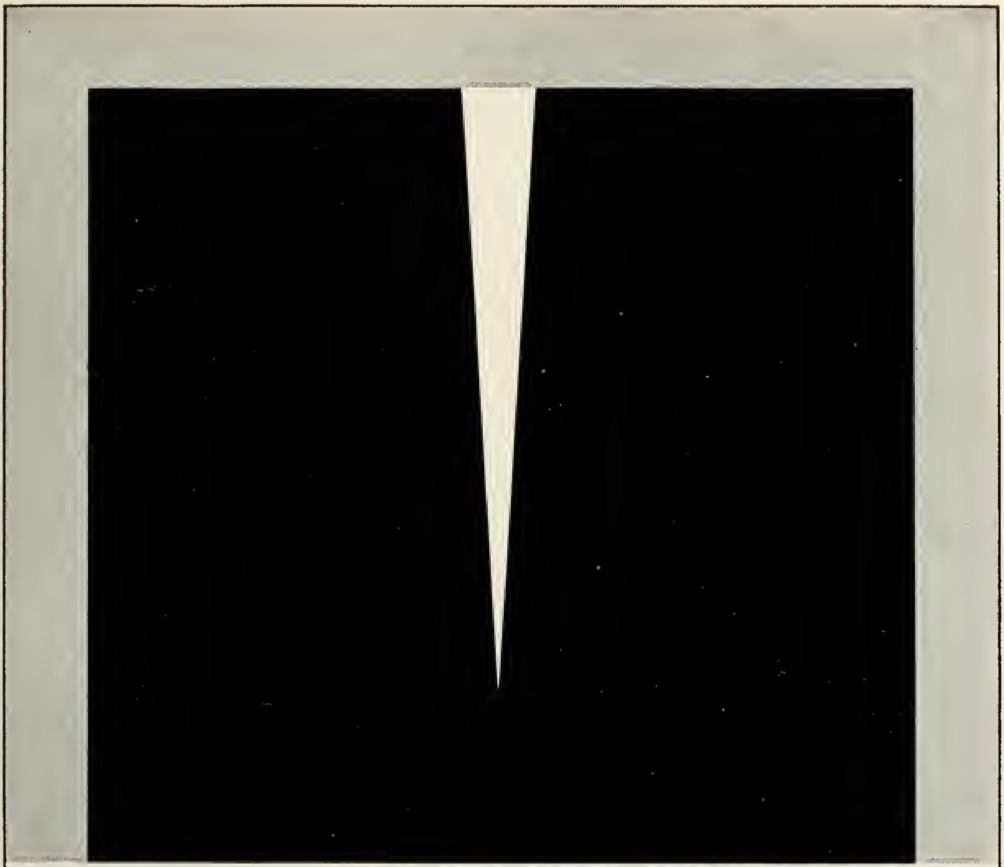

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Disability Decision-Making Theory

WILLIAM ROEMMICH, M.D.

Baltimore

Disability decision-making by inference based upon clinical findings rests upon relationships between these and ability to perform. Chronic disease with resultant impairment is recognizable by clinical findings—symptoms, signs, and laboratory data. As the disease progresses, impairment follows with varying degrees of curtailment in ability to perform.

Recognition and selection of symptoms, signs, and laboratory data form the matrix of a discipline by which disease with resultant impairment and ability to perform can be identified and their future course predicted. *Signs* and *laboratory findings* are independently observable and represent the more credible determinants of these events.

Impairment due to disease has varying magnitudes. These magnitudes are discernible by symptoms, signs, and laboratory findings. There is an inverse relationship between impairment magnitude and ability to perform. Divisibility of impairment magnitude is limited. Divisibility is achievable by selection of symptoms, signs, and laboratory findings.

The specific selections may be considered elements of a set. The theory of sets contributes to the ease and clarity with which probabilities for the existence of varying impairment magnitudes can be defined. Impairment medical determinability may include symptoms but requires signs or laboratory findings. Impairment magnitude has two dimensions—severity and duration—each of which is reflected by symptoms, signs, and laboratory findings.

For disability purposes, a relationship between the biological situations—disease, impairment, and ability to perform—and the nonbiological situation—ability to engage—is obligatory. According to Social Security laws, " 'disability' means inability to engage in any substantial gainful activity because of a medically determinable physical or mental impairment . . . ."

THE MISSION of a disability operation is to select those applicants who are entitled to benefits according to a specific law.

In the Social Security disability program an applicant is entitled to disability benefits if: [1] he has work credits for twenty out of the last forty quarters, [2] he has not engaged for six months because of a medically determinable impairment, and [3] he is unable to engage in any substantial gainful activity by reason of a medically determinable physical or mental impairment which has lasted, or is expected to last, for at least twelve months or ends in death after a six-month waiting period.

IMPAIRMENT EVALUATION IS THE BASIS

There are many factors which prevent a man from engaging. A few of these are: [1] availability of a job, [2] training and vocational preparation for available jobs, [3] past work record, and [4] handicap created by illness or injury. The factors are closely related. Most programs, regardless of which factor is to be considered primary, call upon physicians to measure the amount of handicap. Therefore, most disability programs make heavy demands on physicians, both for acquisition of medical evidence about impairment and for an analysis of the impact which the resulting impairment has on ability to work. Such demands, for reporting and analysis, may appear burdensome to physicians unless they understand the critical role which the reported evidence plays in the assessment of impairment. What role does impairment play in the disability decision?

DISEASE, IMPAIRMENT, AND ABILITY RELATIONSHIPS

Usually, the ability to perform is gradually re-

WILLIAM ROEMMICH *is chief medical officer, Bureau of Disability Insurance, Social Security Administration, Baltimore.*

duced as a result of chronic progressive disease. Because decreased ability to perform due to illness or injury with resultant impairment is required for benefits, disease and impairment may be considered synonymous for disability purposes. Throughout the discussion, I will refer to impairment which always presupposes the presence of significant disease or injury.

Impairment has magnitude discernible as a cause of death or as a cause of reduced ability to perform. A reduction of ability to perform physical and mental activities potentially reduces ability to engage in a job.

As impairment magnitude increases, ability to perform decreases. At some point of time in this inverse relationship, when impairment magnitude becomes sufficiently large, ability to perform disappears. Before ability to perform disappears, it can be considered sufficiently curtailed to result in inability to engage. There are many reasons for inability to engage in substantial gainful activity. Among the many reasons, only impairment-related inability meets the requirement of the disability law. Every disability decision must reflect a critical relationship between impairment and inability to engage. This critical relationship is embraced in the language of the law as "inability to engage in any substantial gainful activity by reason of any medically determinable . . . impairment. . . ."

SIGNS OR LABORATORY FINDINGS REQUIRED

Medical determinability exists only after impairment becomes manifest. These manifestations are: [1] symptoms which only the host can discern, [2] signs which an observer is also able to detect by using normal touch, vision, or hearing, and [3] laboratory findings which require for detection, visual, chemical, psychological, or electrophysiological aids.

An impairment conceivably may have symptom manifestations only. In the realm of long-lasting impairment with resultant significant restrictions of ability to perform, symptoms seldom, if ever, exist without detectable signs or laboratory findings.

In addition to the impairment–inability relationship, the impairment must be medically determinable. Medical determinability, in my opinion, requires, in addition to symptoms, manifestations detectable by an observer and includes anatomical, physiological, or psychological change.

Impairment magnitude, either as a cause of death or as a cause for reduced ability to perform physical and mental activity, can be roughly quantified by means of selected symptoms, signs, and laboratory findings. There are no other determinants by which impairment or reduced ability to perform is measurable.

Signs and laboratory findings are the most credible. In a disability setting, impairment magnitude must, wherever possible, be fashioned by symptoms and signs and laboratory findings. In my opinion, to meet the test of medical determinability, impairment magnitude measurement must include signs or laboratory findings.

The complex relationships between long-lasting impairment, medical determinability, clinical findings, and ability to perform reduce themselves to a relationship between ability to perform and clinical findings.

DECISIONS LEAN ON PROBABILISTIC THEORY

The recognition of ability to perform by symptoms, signs, and laboratory findings reveals a similarity between the judgmental demands on the decision-maker, whether he concerns himself about the existence of disease, on the one hand, or the existence of impairment magnitude on the other. Each situation is fashioned by symptoms, signs, and laboratory findings. The probability for the existence of one disease and the absence of another is progressively increased as the clinical findings characteristic of one and uncharacteristic of the other are expanded.[3]

A group of clinical findings which increases the certainty for the existence of a disease also increases the certainty for the existence of impairment, although not to the same degree. The clinical discipline of a diagnostic process can be applied to the process of determining impairment magnitude. In the diagnostic process, each clinical discovery is considered in terms of the degree to which it increases the probability of one disease and decreases the probability for another. In the process of determining impairment magnitude, each clinical discovery is considered in terms of the degree to which it increases the probability for inability to perform and decreases the probability for ability to perform. In some instances, a clinical discovery has equal relevance for the existence of a disease, on the one hand, and for the existence of impairment magnitude, on the other. In other instances, a clinical discovery's relevance may be higher diagnostically, but lower for definition of impairment magnitude. Whether a group of clinical findings is used to increase the certainty of a diagnosis or the certainty of impairment magnitude, appropriate selection is essential. The magic in each situation exists in a particular combination of clinical findings.

THEORY OF SETS HELPS IN DECISION-MAKING

The clinical manifestations for all diseases may be considered elements of a set.[1] Subsets of such sets may have high diagnostic relevance for specific diseases. Other subsets may have high relevance of impairment magnitude. Therefore, the decision-maker can apply the rigorous logic of set theory to both diagnosis and prognosis.[2] Prognosis may apply either to impairment magnitude as a cause of death or as a cause of reduced ability to perform. In the latter situation, for our program, the decision-maker has at least two points of reference. He has the impairment magnitude reflected by symptoms, signs, and laboratory findings at impairment onset and again at one or more intervals of time—usually six months later. From the symptoms, signs, and laboratory findings at each point of time the decision-maker can assess current impairment magnitude and make a prediction for the future duration.

An example of how clinical findings—elements of a set—can be selected to serve the diagnostic process, on the one hand, and the process of evaluating impairment magnitude, on the other, are:

1. A positive latex fixation has higher diagnostic and lesser functional relevance.

2. A positive tuberculin reaction has higher diagnostic and lesser functional relevance.

3. X-ray evidence of joint destruction has higher functional and lesser diagnostic relevance.

4. X-ray evidence of scattered discrete densities in both lung fields has low diagnostic and functional relevance.

5. If densities in "4" coexist with a history of exposure to silicon dioxide dust (SiO_2), the discovery increases diagnostic relevance but does not change functional relevance.

6. A marked reduction of single-breath uptake of carbon monoxide (CO) has higher functional and lesser diagnostic relevance.

7. Dyspnea has higher functional and lower diagnostic relevance.

8. If the elements of a subset are the clinical findings in 4, 5, 6, and 7, the combination reflects a high degree of certainty for the presence of a specific diagnosis and the existence of significant impairment magnitude.

DECISION CERTAINTY VS. RISK OF ERROR

Impairment magnitude only occasionally can be defined with real numerical precision. That impairment magnitude which results in inability to engage is between two extremes—very small and very large. The problem for the disability decision-maker is to arrive at that magnitude which reduces ability to perform so that the statutory situation—inability to engage in any substantial gainful activity—occurs.

In diagnostic, as in disability, evaluation, the decision-maker must decide when he has enough evidence to assure a sufficient degree of decision certainty. He must decide when the elements of a subset reflect a degree of certainty that the probability for one event is greater than the probability for another. The degree of certainty needed depends upon the risk of error.

CRITERIA INCREASE DECISION CERTAINTY

In both diagnostic and impairment magnitude decision-making, we can agree in advance upon criteria which reflect a sufficient degree of certainty. Elements of a subset which provide a given degree of certainty for one event, as opposed to its contrary, may be considered criteria which reflect a sufficient degree of certainty. Such criteria are represented by diagnostic standards of the National Tuberculosis Association for tuberculosis, the Social Security Administration impairment magnitude listings,* and the American Medical Association's (AMA) impairment guides.[4]

The clinical findings of our listings and those of the AMA impairment guides are believed to reflect impairment magnitude such that ability to perform physical and mental activities has been curtailed. Social Security Administration listings are believed to reflect curtailment of ability to perform to a point equivalent to inability to engage. The AMA guides are believed to reflect several impairment magnitudes and, consequently, several degrees of ability to perform the activities of daily living. In the AMA guides for the musculoskeletal system, there are 100 divisibilities, with a suggestion to use increments of 10. In subsequent issuances, the AMA suggested only four divisibilities.

A first critical test for the AMA guides is whether the symptoms, signs, and laboratory findings for each divisibility (class) actually reflect different degrees of remaining ability to perform. A second is the magnitude of each decrement (class). A first critical test for social security listings (subsets) is whether they reflect a reduction of ability to a point where inability to engage exists. A second is whether the listings (subsets) for the various impairment categories reflect roughly the same degrees of ability-to-perform curtailment.

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*The Social Security impairment magnitude listings mentioned here are currently unavailable for general distribution. Professional groups with program-related interests who desire more detailed information should contact the author.

THREE DISABILITY DECISION-MAKING PROCEDURES

There are definable relationships between the clinical events of illness, resulting impairment, and ability to work. I would like to discuss how these relationships are used by the Social Security Administration in 3 disability decision-making procedures.

The three basic procedures used by the Social Security Administration for disability decision-making are based on the assumption that there is an inverse relationship between impairment and ability to perform. The critical relationship between impairment magnitude and inability to engage is determined inferentially.

1. When an applicant has insured status indicating a recent work record and files a claim stating that he cannot engage due to illness, he has not engaged for six months, he is not engaging, and his impairment manifestations are the clinical manifestations of our listings, we infer that the probability for inability exceeds that for ability. The probable inference is impeached only by a finding that he is actually engaging. This represents one decision-making process.

2. An examination of our listings will reveal that these include a limited number of impairments. There are a limited number of subsets for each impairment. There are listings only for single impairments. To make decisions for unlisted and multiple impairments, we use a second decision-making process. An inference that the applicant has inability to engage due to impairment may be made also on the basis of a medical judgment that unlisted groups of symptoms, signs, and laboratory findings present in one or more impairments of an applicant represent impairment magnitude range similar to that reflected by the listings. An inference is again made that the probability for inability to engage is greater than the probability for ability to engage. This second decision-making process embraces all the relationships of the first, except that threshold values are determined for each situation by the evaluator. This is the second decision-making process.

3. If clinical findings of an applicant's impairment are unlisted and, in the physician's judgment, represent lesser impairment magnitude and curtail ability to engage less, a third decision-making process occurs.

The first two decision-making procedures are based upon discernment of a single impairment magnitude. This magnitude is present in applicants whose symptoms, signs, and laboratory findings are listed. This magnitude is present also in some applicants whose symptoms, signs, and laboratory findings are not listed, but medical opinion holds that these, nevertheless, curtail ability to perform so that the claimant's allegation of inability to work is reasonable. In all applicants whose clinical findings are listed or represent such similar impairment magnitude, a medical and administrative inference is made that inability to engage exists by reason of a medically determinable impairment. After applying procedures 1 and 2, there remain applicants whose clinical findings are believed to reflect smaller impairment magnitudes.

The third decision-making process can be achieved in 2 ways:

1] Remaining ability to perform physical and mental activities is actually measured. This remaining ability to perform physical and mental activity is compared with the physical and mental activity demands of a group of jobs which the applicant is able to do by virtue of vocational preparation, education, and work experience. If remaining ability to perform physical and mental activity exceeds job demands, the relationship of impairment to inability does not exist. If the ability to perform is smaller, the relationship is there.

This first way of doing the third decision-making procedure requires an actual measurement of remaining ability to perform physical and mental activities. In a few situations, such a measurement can be achieved. In impairments such as lung failure or loss of visual acuity, there are laboratory findings which can be translated into degrees of ability to perform. In other situations where the limiting manifestation of ability to perform is pain only, weakness only, or nervousness only, it becomes a question of assessing intensity of the symptom. The decision-maker must depend upon a symptom which is appreciated only by the host. Likewise, the symptom's intensity can be appreciated only by the host. In my opinion, symptom manifestations alone do not fulfill the criteria of medical determinability. There should exist observer-detectable signs or laboratory findings.

2] If, on the other hand, the decision-maker applies inferential measurement of impairment magnitude as in the first and second process, now the elements of a subset must achieve additional divisibilities of impairment magnitude. It must be a lesser magnitude than that reflected in the listings where procedures 1 and 2 are applied. A single additional division actually results in 2 impairment magnitudes—1 larger and 1 smaller. Both are smaller than the impairment magnitude reflected by the listings. The evaluator can now infer the appropriate relationship of impairment to inability for all applicants whose impairment meets the new larger magnitude yet is smaller than that reflected by listings. Such a procedure would erase the necessity for the previous listings because inferences under procedures 1 and 2 would now flow from this new and lesser impairment magnitude.

To escape this voiding of previous levels and thus changing the level of severity for all applicants, this new magnitude must be applied selectively. If it applies selectively on the basis of job demands, one must be able to [1] recognize degrees of job demands and [2] relate this new impairment magnitude with these demands. Such a process requires, for each job demand magnitude, a corresponding impairment magnitude. This process can be carried on indefinitely. To do so, we must achieve a progressive divisibility of impairment magnitude and job demand magnitude, unless the critical relationship of impairment to inability is modified.

At best there are only 10 divisibilities in some diseases and fewer than 4 in others. If the impairment magnitude reflected by the listings falls on the extremes of the lesser magnitudes, further divisibility may not be possible.

SUBSETS AS UNITS OF IMPAIRMENT MAGNITUDE

Subsets, the elements of which are clinical findings, may form the basis for dividing impairment magnitude. The social security listings, as they are used currently, define a single impairment magnitude. In the presence of this impairment magnitude and in the absence of work, we make an inference in favor of an applicant. In its absence, we do not. To make decisions in its absence with the third procedure, the decision-maker must achieve as many divisibilities of impairment magnitude as required by the range of job demands.

It may be that the listings technique using only procedure 1 and providing only a single impairment magnitude is sufficient for decision-making purposes if the magnitude is appropriately defined. Listings reflecting one impairment magnitude would suffice for all decision-making if, after such ability-to-perform curtailment, the applicant's choice of jobs offered a sufficiently wide range of activity demands so that, with his remaining capacity, he could perform.

In any event, classification of clinical findings into subsets, the elements of which are signs, symptoms, and laboratory findings, may provide us with a probabilistic tool penetrating enough to achieve more than one divisibility of impairment magnitude. This tool may also achieve sharper outlines for single impairment magnitudes. Either achievement will create greater equity, uniformity, and decision repeatability. Decision repeatability—all else being equal—is perhaps the best measure of decision validity we have today.

SUMMARY

1. Severe, long-lasting disease produces varying degrees of impairment and variously curtails man's ability to perform physical and mental activity.

2. In significant reduction of ability to perform physical and mental activities, there is reduction of ability to engage.

3. Impairment magnitude is recognizable by selected combinations of clinical manifestations—symptoms, signs, and laboratory findings.

4. Impairment may be manifested by symptoms alone but becomes medically determinable only when observable signs or laboratory findings are coexistent.

5. When impairment reduces ability to perform sufficiently, it results in inability to engage.

6. All social security disability decisions must reflect a critical relationship between impairment and inability.

7. In the listings technique for disability decision-making, only the impairment magnitude requires definition. The other—ability to perform—follows as a probable inference. That ability to perform which remains when the impairment magnitude is reflected by the clinical findings in the listings is sufficiently large, we believe, to result in inability to engage in any substantial gainful activity, except where the applicant is actually engaging.

8. In the set of all symptoms, signs, and laboratory findings are subsets which provide degrees of certainty for the existence of specific diseases, on the one hand, and impairment magnitude, on the other.

9. More than one subset can reflect similar impairment magnitude (definable as correlation coefficients).

10. The elements of subsets may be so chosen that they reflect unequal impairment magnitude.

11. The same subset cannot reflect unequal impairment magnitudes so that inability exists for some applicants and does not exist for others.

(Continued on page 458)

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The Thymus

ESTHER M. GREISHEIMER, Ph.D., M.D.
Philadelphia

WHEN THE AUTHOR was a medical student, as well as during many succeeding years when she was teaching physiology, the information regarding the functions of the thymus left much to be desired. The textbook assigned by the department to the students at the time of the author's retirement from the teaching of medical students did not even include "thymus" in the index.[1] A later edition of the same textbook[2] includes three references to the thymus which will be given here only to stress the meager information appearing in a standard textbook. In the first (p. 508), the thymus is included with spleen and lymph nodes as a secondary site of hemopoietic activity; the three sites are described as "transitory and of little importance." No mention is made of the thymus (p. 521) in the discussion of the origin of the lymphocytic series or in the discussion of lymphoid tissue (p. 770). The second place in which the thymus is mentioned is in adrenal insufficiency, in which the thymus is enlarged (p. 1086); the involutional changes characteristic of fasting, trauma, and other stresses do not occur in the absence of adrenal cortical function. The third reference is in connection with the administration of oxycorticoids, in which it is stated that the thymus undergoes drastic involution (p. 1096).

It is known that the thymus grows rapidly in embryonic life and that it is the first organ in the body to become lymphoid in structure. It attains its greatest relative weight in the newborn infant, at which time the average weight is 11 gm. It continues to grow throughout childhood and attains its maximum absolute weight of 35 gm. at about 12 years of age. Growth ceases early in adolescence and involution begins and continues into old age, when the thymus weighs less than it does at birth.

STATUS LYMPHATICUS

The question of status lymphaticus was a puzzling one for a long time. Ewing[3] stated that the anatomical features of the "lymphatic constitution" were believed to be hypoplasia of the heart and aortic system of vessels and partial or general hyperplasia of the lymphatic organs (thymus, spleen, lymph nodes, and lymphoid or red bone marrow). Ewing pointed out that although the lymphatic constitution had been recognized for several years by pathologists of the Vienna school, it had received very little attention elsewhere. The lymphatic constitution was believed to be responsible for sudden deaths of many children and of many individuals under chloroform anesthesia. However, Ewing felt that the observations made by him were too few to demonstrate the truth of the hypothesis that connected a large group of sudden deaths with a simple hyperplasia of lymphatic structures.

Despite Ewing's doubts, the concept of status lymphaticus gradually spread and continues to occupy space in some standard textbooks.[4,5] Even in 1965 we are assured that there is "no room for doubt that the constitutional disturbance known as status lymphaticus is a real entity."[6] By rights, status lymphaticus should have been laid to rest after the report in 1931 of a collective investigation on status lymphaticus, organized by the Medical Research Council in conjunction with the Pathological Society of Great Britain and Ireland. The report stated that "in the opinion of the Committee the facts elicited in the present inquiry afford no evidence that so-called status thymicolymphaticus has any existence as a pathological entity."[7] Dodwell wrote twenty-three years later, with feeling, of the spread of the "myth" of status lymphaticus.[8]

Fisher (p. 689)[9] points out that more accurate determinations of the cause of death are "chiefly responsible for the final exodus" of the concept of status thymolymphaticus from medical attention.

ESTHER M. GREISHEIMER *is professor emeritus of physiology, Temple University School of Medicine, Philadelphia, Pa.*

ORIGIN AND DEVELOPMENT OF THE THYMUS

Beard did a remarkably fine piece of work on the origin and development of the thymus in Raja batis (the common skate, one of the largest British species, which may reach a weight of 500 lb. in the adult). Beard[10] called attention to the fact that Koelliker had previously discovered the origin of the thymus in mammals (rabbits) from the epithelium of a gill pouch and had noted that the original epithelial cells gave rise to leukocytes (1879), but his work had been ignored. Beard's observations were made on embryos of the skate, as they grew from 6 to 70 mm. in length. The first appearance of a bit of modified epithelium, just above the opening of the first branchial cleft in 6-mm. embryos, represented the rudiment of the thymus. The first leukocytes were formed in embryos of 14 to 17 mm.; Beard described the gradual conversion of epithelial cells of the thymus rudiment into leukocytes.[11] No leukocytes are present anywhere else in the body of the embryo at this time. At 22 mm., the formation of leukocytes is proceeding apace in the thymus, and some gration of leukocytes is conspicuous. The production of leukocytes becomes more abundant By the time the embryos are 25 mm. long, emiare wandering into the surrounding mesoderm. and the emigration more prominent until the 70-mm. stage is reached. Beard was convinced that the parent source of all of the leukocytes was the thymus, but he wrote,[11] "And, indeed, has it yet fallen to the lot of any writer upon the thymus to write the truth and to be believed?!!"

More than half a century later, Auerbach has contributed additional information of great value on the development of the thymus. He has found that both the epithelium and the surrounding capsule of mesenchyma which are present in twelve-day mouse embryos are essential to the complete development of the thymus.[12] He confirmed the fact that the lymphoid tissue of the developing thymus originates in the epithelial component of the early thymic rudiment. He was convinced that the mesenchyme furnishes the initial "inductive" stimulus, as well as the stromal elements of the thymus.[13] Auerbach found that the lymphoid cells are nonadhesive, in contrast to other thymic cells; they eventually leave the thymus and are disseminated throughout the body in a selective manner. He suggests that as they settle in their new environments they become foci for the production of antibody-forming cells. Thus, the hypothesis proposed by Auerbach is that the thymus represents the major primordium[14] of the mammalian immunological system. Could Beard have been making a long, long shot in the dark when he thought that the leukocytes were formed in the thymus for the purpose of guarding the gills from bacteria?[11,15]

So far as the spleen is concerned, Auerbach found in his work with embryonic spleen explants that the spleen cannot self-differentiate.[16] It requires a cellular contribution of the host, in other words, the thymic influence, in order to differentiate into lymphoid tissue.

ROLE OF THE THYMUS IN IMMUNITY

Miller and Davies[17] have reviewed the embryological development of the immune mechanism. Immune phenomena, which include antibody production against microbial antigens or recognition of foreign tissue cells, are limited to vertebrates. The beginning of immunological responses corresponds in time to the first appearance of lymphocytes in the embryo. The thymus in man is an epithelial structure until the end of the second month of intrauterine life, at which time it acquires a mesenchymal component. Although lymphopoiesis is of epithelial origin, there needs to be intimate contact with mesenchyme, as shown by Auerbach.[12]

Differentiation into cortex and medulla and the formation of Hassall's corpuscles begin in the human embryo of 50 to 60 mm., during the third month of intrauterine life. Mitotic activity is marked in the thymus during the remainder of intrauterine life but is absent or minimal in peripheral lymphoid structures until after birth.

Miller and Davies suggest that lymphocytes migrate out from the thymus to circulate in the blood and lymph, and only when antigenic stimulation occurs do they accumulate to form independent colonies in the spleen, lymph nodes, Peyer's patches, and other gastrointestinal lymphoid tissue.

If the thymus is removed in early life, before the immune apparatus is developed, there is poor development of the peripheral lymphoid structures and marked disturbances in immune functions of the body. Miller and Davies[17] list 5 possible phases in the embryological development of the immune mechanism. These are [1] the inductive phase, during which the mesenchymal and the epithelial elements interact to produce the first lymphoid tissue, [2] the production of nonadhesive lymphoid cells, [3] the migration of lymphocytes into blood and lymph, [4] selective settling in spleen and other peripheral lymphoid organs to form colonies, and [5] the possible elaboration by epithelial-reticular cells of the thymus of a humoral factor that enables lymphoid cells in the various peripheral lymphoid organs to become "competent from the immunological standpoint."

Not all scientists accept the role of the thymus in immunology. Miller[18] states the reasons for this. The first reason is that antibody formation has not been demonstrated in the normal thymus. The second reason is that even after intense antigenic stimulation, plasma cells, which are the morphological evidence of active antibody formation, and germinal centers are not found in the thymus. The third reason is that thymectomy in the adult animal has little or no significant effect on antibody production.

Having spent most of her life in academic circles, the author seems unable to resist making the following analogy. Perhaps the thymus, with professorial rank, plans and supervises the body's responses to antigenic stimulation but leaves the execution of the elaborate plans to the assistant professors (spleen and gastrointestinal lymphoid tissue) and the instructors (peripheral lymph nodes). It will be evident, as we continue, that should the professor be absent or wanting in planning and supervisory ability the response to antigenic stimulation can go awry and other evidences of immunological abnormalities may appear, as can happen in the finest universities.

Miller[19] found that after neonatal thymectomy mice, rats, and hamsters die of so-called wasting disease. A striking anatomical feature of this condition is a deficiency of small lymphocytes in the blood, spleen, Peyer's patches, and lymph nodes. The antibody response is depressed and there is permanent impairment of the ability to reject skin grafts from donors of foreign strains. So far as adult mice are concerned, if they are thymectomized and the whole body irradiated, there is no recovery of lymphopoietic and immune functions. This seems to be sufficient evidence that the adult thymus is still essential to reestablish immunological mechanisms when the immune apparatus has been injured.[20] It also raises questions regarding the possible relationship between the thymus and certain immunological abnormalities in man.

Miller[21] believes that there is evidence of a humoral thymus mechanism involved in the maturation of immunologic capabilities. He suggests that such a factor may be "required either for stimulating the proliferation of immunocompetent cells or, as seems more likely, for inducing the differentiation of stem cells to lymphoid cells, which can then participate in immune reactions." Is this humoral factor comparable to a dean or an executive vice-president urging the professor to secure grants so that his associates may carry out their research obligations?

In view of the many facets of research being carried out in various places and on various species, as well as study of clinical cases that appear to have some connection with the thymus, it seemed advisable to call a conference on the thymus. Therefore, the first Conference on the Thymus was arranged and held at the University of Minnesota late in 1962. The proceedings of the conference have been edited by Good and Gabrielsen.[22] Several of the remaining excerpts deal with material from this source.

THE BURSA OF FABRICIUS

In 1956, it was reported that the bursa of Fabricius plays an essential role in the development of immunologic capacity during the early life of the chick. The importance of this structure and its comparison with the thymus is dealt with by Ackerman and Knouff,[23] Glick,[24] and Warner and Szenberg[25] in the conference proceedings.

CLINICAL CONSIDERATIONS OF THE THYMUS

Good and associates[26] have made a very provocative and speculative suggestion that there may be failure of the immunological apparatus at different levels. According to this challenging concept, the most central failure would be represented by a deficiency of the epithelial rudiment (as in the Swiss type of agammaglobulinemia); failure at intermediate levels would be represented by lack of appropriate mesenchymal induction of lymphoid tissue (as in ataxia telangiectasia), by failure of the development of the so-called nonthymic central lymphoid tissue of the gastrointestinal tract (as in the sex-linked, recessive form of agammaglobulinemia) and, finally, by failure at the peripheral level, involving the lymph nodes (as in acquired agammaglobulinemia, with thymoma).

In the lymphopenic or Swiss type of agammaglobulinemia, the thymus is small and abnormal in structure. The abnormalities include lymphocytophthisis, extreme lymphopenia, failure of development of peripheral lymphoid tissue, agammaglobulinemia, and extreme susceptibility to a variety of infections. The disease is familial and apparently is transmitted as a simple Mendelian autosomal recessive trait. It occurs in both girls and boys, and so far as is known, the survival period is limited to 18 months of age[27] (p. 17). This condition may be due to a defect in the development of the epithelial rudiment of the thymus, and the failure of the peripheral lymphoid tissue may be secondary to this defect. If we pursue the analogy, the professor himself is at fault, having had inadequate training for the work undertaken.

The association of ataxia telangiectasia with a defective thymus is gaining attention. In this condition, there is a progressive cerebellar ataxia which begins early in life and completely incapacitates the patient by the age of early adolescence. The telangiectasias involve the bulbar conjunctiva and many cutaneous areas. The condition is familial and appears to be inherited as an autosomal recessive. In some of these patients, the thymus is like that of an early embryo, before lymphoid induction by mesenchyme has occurred. However, the deficiency is quantitative, and one does not always find a uniform defect in the thymus.[28] Some authors do not agree that ataxia telangiectasia is an expression of thymic dysfunction.[29] This condition may be analogous to academic circles in which the professor is not supported in his projects by the dean and executive vice-president.

The largest group of agammaglobulinemic patients is the one with the sex-linked recessive form of the disease. These patients have a low level of gamma globulin and form essentially no antibody to antigenic stimulation. The thymic tissue is relatively normal, but all the other lymphoid tissues, including the tonsils, Peyer's patches, and appendix, are very small, abnormal in structure, and poor in lymphoid cells[26,27] (p. 12). This condition occurs only in boys. There is an absence of plasma cells and a failure of plasma-cell response to the most intense antigenic stimulation. These patients are very susceptible to bacterial infections after 6 months of age.[30] This is analogous to a situation in which the professor, despite preparation, fails to gain the confidence and cooperation of his associates.

Several cases of acquired agammaglobulinemia with thymoma have been reported. In one case reported by Good and associates[27] (p. 7), the thymoma weighed 565 gm. In a more recent case report, the thymoma weighed 950 gm.[31] Good and associates suggest that the thymoma may be a compensatory tumor indicating a lack of appropriate feedback control from a defective peripheral lymphoid tissue.[26] This is analogous to a situation in which the professor works long hours overtime, since he is not kept informed of the work, if any, that is being done by his associates. In other words, it is an example of breakdown of effective communications.

This concept of failure at different levels of the immunological mechanism is a most exciting one; we now eagerly await further evidence before we make decisions about it.

ASSOCIATION WITH OTHER CONDITIONS

The history and present status of the relationship between the thymus and myasthenia gravis are amply reviewed by Fisher[9] (pp. 690-695), who states that the "precise nature of the relationship between myasthenia gravis and the thymus remains to be elucidated." Hess and associates[32] (pp. 668-674) present evidence that seems to indicate that autoimmune phenomena occur in myasthenia gravis. Lymph follicle formation and the presence of plasma cells are noted in a large percentage of patients with myasthenia gravis.

Fisher[9] (p. 691) points out the fact that lymph follicle formation is not specific for myasthenia gravis; it occurs also in patients with Addison's disease, thyrotoxicosis, acromegaly, and gonadal hypofunction.

On the other hand, thymic atrophy is present in Cushing's syndrome, and the administration of cortisone has thymolytic effects.[33]

THYMUS AND LEUKEMOGENESIS

The role of the thymus in leukemogenesis is discussed by Furth and associates.[34] Leukemia in a high leukemic strain (Ak) of mice originates in the thymus, at 4 to 6 months of age. The leukemic cells soon enter the blood and colonize in many organs. The removal of the thymus in this strain of mice at 6 weeks of age decreases the incidence of leukemia and thereby prolongs life.

The thymic lymphoma virus was discovered by Gross in 1951. It was found soon thereafter that thymectomy prevented viral lymphoma. Other factors reduced the incidence of thymic lymphoma also. Stress, such as pneumonia, apparently reduced the incidence by causing involution of the thymus. The administration of cortisone inhibited the occurrence of spontaneous lymphoma in mice of the high leukemic strain. The incidence of radiation-induced lymphoma was decreased if cortisone was administered after irradiation. Even drastic underfeeding decreased the incidence of lymphoma, due to the involution it produced in the thymus.

On the other hand, thymic grafts in thymectomized mice favored the appearance of leukemia of the spontaneous type, as well as that induced by carcinogens, radiation, and virus.

The authors state that in their "current thinking on thymic lymphomagenesis the virus and TFL (thymic lymphoma factor) are intertwined; however, their precise interrelationship is unknown."

With respect to human disease, Simmons[35] thinks that the thymus plays an important role in the genesis and perpetuation of leukemia. Fisher[9] (pp. 679-686) lists the following types of thymoma: the first is the pure lymphocytic lymphoma, of which there are very few authenticated reports. The second is the pure epithelial tumor of the thymus, such as is seen in myasthenia gravis and Cushing's disease. A variant of this is the epithelial spindle-cell tumor which occurs more frequently in the thymomas associated with hemopoietic insufficiency. The third is the mixed lymphocytic and epithelial, which is the most common type of thymoma. The fourth is the granulomatous type, which morphologically resembles Hodgkin's disease except that the giant cells stain with the periodic acid–Schiff technique (described in Ham and Leeson[36]). The fifth is the squamous-cell carcinoma and the sixth is the thymolipoma.

Fisher reminds us that the criterion of malignancy of a thymic tumor is the presence of metastases, which are confined almost exclusively to intrathoracic structures.

In closing, it seems important to mention a few remarks made by Trentin[37] in his summary of the conference. He reminds us that we do not yet have a complete understanding of the normal physiology of the thymus. In addition to its role in immunology it may have nonimmunological functions. The fact that sepsis has not been noted in young animals dying of wasting disease after thymectomy has not been explained. Perhaps this is indicative of a metabolic function. Surely, the adult thymus plays an important role, despite its involution, since there is no regeneration of lymphoid tissue in spleen and lymph nodes in adults following irradiation of the whole body.

Another question of fundamental importance is "Does the thymus perform its immunological functions by means of a humoral or a cellular mechanism, or both?"

It is stimulating to know that despite the giant strides made in the last few years with respect to the thymus, there is still a great deal to learn.

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A Psychiatric Viewpoint of Cerebral Vascular Accidents

RUSSELL O. SAXVIK, M.D.
Bismarck

THE 68-YEAR-OLD gentleman spoke weakly into the phone, "Doctor, I hate to tell you this, but I'm going mad, completely mad, and I'm afraid." So began a contact with a man who, four weeks before, had suffered a cerebral accident.

Premorbidly, this successful businessman presented a pattern of normalcy. He now disclosed a pathologic picture of a person with transient episodes of disorientation, bursts of thought confusion and memory loss, and decreased intellectual functions. His judgment vacillated as did his emotional tone. At times, he had sudden outbursts of weeping; at other times, he made disclosures of trivial incidents of his life that now made him remorseful. For no obvious reason he would sometimes falsify his present life with circumstantial tales that were obviously untruths.

Although this man now demonstrated no particular gross motor or sensory loss, his draw-a-person projection test indicated a severe distortion of his body image. In fact, with obvious bewilderment, he was unable to complete a head with a face. He became quite irritated and said he never could draw and this was all foolish anyway. The impact of not feeling his body as it formerly existed frightened this man terribly. The loss of his "me" feelings created growing anxiety and depression to the point that he expressed death wishes.

This damaged individual recognized his emotional state, but more often than not the stroke patient does not accept the facts of his illness and will strongly defend his feelings by rigidity and impaired quiddity. The identical problem is seen in the transient ischemic episodes of cerebrovascular insufficiency.

It is important for the physician to recognize in the stroke patient the almost universal experience of episodes of depression or anxiety. This usually will occur in the third to fifth week from the onset of the insult to the brain, when the patient becomes aware of the awful truth that he is no longer the same person, that he is disabled and apt to remain so. It is always right to acknowledge, with sincerity, the patient's disturbed feelings and allow him time to express them. It is also the physician's responsibility to recognize a patient's denial of the true facts of the damage and assist him to overcome his optimism for an impossible recovery. One must, however, be cautious in being too blunt or too energetic in breaking through a denial as the depression behind it may be of serious to dangerous proportions.

For the most part, the average stroke patient's emotional swings cause no real management problem for the physician. There are, however, several types of patients who present problems.

These are:

1] *Those who suddenly become paranoid and behave in panic.* Their psychoses emerge out of their personalities and their delusions usually revolve around ideas of persecutions. They often exhibit much bitterness and hostility and will attack their "enemies" if they feel the threat is overpowering. It is not unusual that they will turn on themselves with destructive acts if they feel there is no escape from the "tormentors." Without question, these patients must be hospitalized and energetically treated.

2] *Those who become progressively more depressed with symptoms of sleep irregularities, disinterest in eating, and marked diminution of interests.* They may become quite agitated or manifest psychomotor slowing. Withdrawal is a common symptom. Their thoughts are consistent with their black moods and often center on unrealistic ideas that they are utterly worthless, a terrible burden to their families. They offer in-

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RUSSELL O. SAXVIK *is a psychiatrist, Quain and Ramstad Clinic, Bismarck.*

numerable somatic complaints as if consumed with incurable or fatal diseases. Suicide is always imminent and often carried out. These patients usually require hospitalization and for the most part can be lifted from their depressed states with chemotherapy.

3] *Those who maintain a rigid, often ridiculous, denial of their disability.* They refuse all attempts of rehabilitation. These stroke patients usually are of the younger age group, often have a family to support and, with proper training, have potential to return to work. They will vigorously uphold the idea, "I'm all right and can stand on my own two feet." These persons frequently have the characteristics of being too conscientious, too hardworking, too unemotional, and too active in being strong and independent. Any sign of weakness is taboo and they will resent all attempts to help. These patients do best in a rehabilitation center with good psychotherapy available.

4] *Those who tend to become parasitic and are motivated more toward illness than toward a desire for healthy activity.* These patients produce symptoms far greater than physical findings warrant. They are complaining, demanding, and easily hurt or angered when their excessive demands are refused or unfulfilled. They shape a family relationship by immobilizing the family's activity to center on themselves. The spouse often becomes worn out, bitter, and frustrated, with thinly veiled animosity as the result of control by the helplessness imposed by the patient. Actually, such intense family suffering can be created that often the only solution is family counseling or a separation of the stroke patient by placement in a nursing home or similar facility.

In all four categories, it is the responsibility of the physician to offer more than the usual routine encouragement and support. Family attitudes must be molded or shifted; often, the patient must be rehospitalized to protect himself or those about him. Medication is essential in controlling anxiety or depression, and, finally, rehabilitation opportunities can offer the stroke patient the chance to return to a useful and comfortable life. When his psychological needs are overlooked, a person with a cerebrovascular accident can otherwise, too often be relegated to a state of nothingness.

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12. The selection of elements for subsets which reflect impairment magnitudes is possible from medical experience.

13. The rate of impairment magnitude change is predictable from the elements of a subset, and these elements may be the same as those which reflect impairment magnitude.

14. Between birth and death, man may achieve incredible ability, always vulnerable to the ravages of disease and almost indestructible because of the power to heal. The decision-maker must reckon with this complex relationship as a function of time. The situation at any point in time is reflected by symptoms, signs, and laboratory findings.

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Paralytic Brachial Neuritis

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JOSEPH A. RESCH, M.D.

Minneapolis

DURING WORLD WAR II a previously unrecognized brachial neuritis was described in military personnel of various countries. Spillane[1] collected 46 patients under the designation "localized neuritis of the shoulder girdle." Parsonage and Turner[2–4] expanded the clinical description and retitled it neuralgic amyotrophy in a separate series of 136 military and 82 civilian patients. Individual patients of Bernard and Fox,[5] Richardson,[6] and Wyburn-Mason[7] also fit into this group. Recently Magee and Dejong[8] described similar cases and directed attention to the disorder in the United States. Because we have seen 7 patients with this type of brachial neuritis since our recognition of case 1 nine months ago, we assume that it is more common than previously realized by most physicians. This report adds an observation on the method of onset which permits speculation as to etiology. It also indicates the use of electromyography for diagnosis and following the course of recovery in this syndrome.

The clinical picture is easily recognized. The first symptom is sudden onset of severe pain in the shoulder radiating to the scapula or for varying distances down the arm. This is first noticed, as a rule, when the patient awakens from sleep. Within a few days the pain lessens in intensity and paralysis of one or several muscles ensues. Paralysis is most frequent in the deltoid, spinati, and serratus magnus muscles, but other muscles may be affected. If sensory loss develops, the skin area supplied by the axillary nerve is most commonly affected.

CASE REPORTS

Case 1. In December 1958, a 28-year-old missionary pharmacist stationed in Ethiopia awoke with severe burning superficial pain in the left shoulder over the deltoid muscle. The intensity of the pain remained constant for one week. It then diminished in severity. Some time during the week he noticed loss of sensation in the same area. On the third day after onset of pain, he developed disabling weakness of abduction of the left arm. A neurologist was consulted on the fourteenth day. At this time prednisolone, vitamins B_1 and B_{12}, and electrical stimulation of the muscle were instituted in treatment. The pain subsided in one month. Muscle strength became normal in six months.

The next attack occurred eighteen months later when he again awoke with similar pain over the right scapula. This was followed in a few hours by an ill-defined decrease of sensation and severe weakness of extension of the right arm at the shoulder. There was also winging of the right scapula. The patient began taking prednisolone seven days after onset. Complete recovery occurred in three weeks.

The third episode began six months later and was similar in onset and location to the second. However, it did not progress to paralysis or sensory loss. The pain subsided spontaneously within twenty-four hours.

The final episode commenced on Oct. 6, 1964 when he awoke from a nap and experienced pain in the right shoulder below the outer one-half of the clavicle. Prednisolone was begun the next day. A total of 33 mg. were used during the next fourteen days. When he arrived at University Hospitals on Oct. 20, the pain had ceased. The clavicular portion of the right pectoralis was slightly smaller than the left and fasciculations were evident in the smaller muscle. Minimal weakness was found on adduction and abduction of the right arm and external rotation of the left shoulder. The muscle stretch reflexes were symmetrical and normal. Electromyography revealed the presence of fasciculations in the right pectoralis muscle but was otherwise normal. Motor unit action potentials (M.U.A.P.s) were normal in all muscles of the shoulder girdle with the exception of the left deltoid. In that muscle there were a decreased number of M.U.A.P.s firing in proportion to the strength of contraction. Some of these were slightly large in amplitude. Conduction velocity was normal in the right ulnar and right median nerves. Conduction time to the right pectoralis and both deltoid muscles was considered normal when the brachial plexus was stimulated in the supraclavicular fossa. A repeat electromyogram seven days later was unchanged.

Laboratory values for hemoglobin, total and differential white blood cell count, total blood protein, blood urea nitrogen, erythrocyte sedimentation rate, and urinalysis were all normal. The cerebrospinal fluid was not examined.

WILLIAM R. KENNEDY *is assistant professor of neurology, and* JOSEPH A. RESCH *is professor of neurology, Division of Neurology, University of Minnesota, Minneapolis.*

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This case illustrates that an individual patient may be subjected to repeated episodes affecting different locations. It also raises the question of possible benefit from steroid therapy in acute cases.

Case 2. A 48-year-old man previously known to have mild diabetes and temporal lobe epilepsy, was seen in July 1964, complaining of pain in both suprascapular areas. He could not recall details of the onset of pain, but weakness of the left shoulder had begun two months previously. On examination the left deltoid muscle seemed smaller than the right. The muscles which externally rotate the left shoulder were weak. The patient experienced pain when that arm was abducted higher than 45°. This pain was thought to be due to "frozen" shoulder. The muscle stretch reflexes were slightly hyperactive but equal bilaterally. There was no sensory loss by history or examination.

Electromyography revealed large numbers of fibrillation potentials and absence of voluntary M.U.A.P.s in the left supraspinatus muscle. There were a decreased number of M.U.A.P.s for the strength of contraction in the left infraspinatus and left deltoid muscles with some increase in insertion irritability of the former muscle. Motor conduction velocity was normal in the right ulnar and right median nerves.

Hemoglobin, white blood cell count, alkaline phosphatase, cerebrospinal fluid, and roentgenograms of chest and shoulders were reported as normal. The sugar content of a fasting blood sample and a urine specimen was elevated.

The patient returned in November 1964. Although he felt there was mild residual weakness, muscle strength testing and electromyography were normal.

This man presented with shoulder pain which was probably secondary to immobilization and correctly diagnosed as "frozen" shoulder. The diagnosis of the primary condition was overlooked before performance of electromyography. This test is useful and at times necessary to corroborate the clinical diagnosis of paralytic brachial neuritis.

Case 3. In June 1964, a 47-year-old male construction worker awoke with severe pain in the left shoulder over the deltoid muscle. In a few days the pain assumed an aching character and then spread to the scapular areas and also down the radial aspect of the arm to the dorsum of the hand. At about this time, he found that he could no longer lift his arm above waist level. Strength in the hands was normal. He also noticed a decrease in sensation over the lateral aspect of the shoulder. By July pain was present only during movement and was relieved by heat. The patient's self-diagnosis was bursitis. In November his strength began to return and the intermittent pain improved. When first seen by us in January 1965, there was minimal weakness of the left deltoid, left biceps brachei, and left pectoralis muscles. Winging of the scapula was not present. Sensation was intact.

An electromyogram in January was essentially normal. Conduction velocity in the left ulnar and left median nerves was normal. Conduction time from supraclavicular fossa to the right and left deltoid muscles was equal.

The hemoglobin, white blood cell count with differential, blood protein, blood urea nitrogen, urinalysis, and cerebrospinal fluid were normal. Roentgenogram of the chest was normal while that of the cervical spine showed a slightly narrowed disk space between C5 and C6. The myelogram was normal except for the cervical area. The report stated that "there were consistent defects, a bigger one at the level of C7-T1 on the left side—these could represent herniated disks."

In 1957 he had experienced similar pain in the right shoulder which had been diagnosed as bursitis. There had been no weakness at that time.

This case illustrates the typical history with the frequent complication of "frozen" shoulder. In these cases the duration of the initial pain is unknown because of the superimposed pain accompanying this complication. It is interesting that the patient told each of 4 physicians who had occasion to take separate histories that he had awakened with the pain. Yet none had incorporated this fact into their written interpretation of his history.

Case 4. In August 1958, a 32-year-old soldier awoke from a nap in the back seat of an automobile with severe aching pain in both shoulders. Within twenty-four hours, his speech was barely audible. A few days later the return to normal volume was accompanied by hoarseness. On the second day he found he could not elevate his arms above his head. He was on leave at the time and the home physician prescribed applications of hot compresses.

When he was examined at his base hospital three weeks later, the pain had disappeared. Weakness was manifest in both triceps, both biceps, the abductors of both arms, the extensors of the left arm at the shoulder, and the external rotators of the right arm. There was atrophy of the left spinati and winging of the right scapula. The right vocal cord and left diaphragm were paralyzed. A punctate erythematous rash was seen over both forearms and both legs. A provisional diagnosis of acute poliomyelitis was made. One examiner included in his differential diagnosis the Parsonage-Turner syndrome. Electromyography revealed partial denervation of the trapezii, supraspinati, and left infraspinatus muscles. Examination of the cerebrospinal fluid was normal on 2 occasions. LE clot tests were negative. The pathological report of biopsy from a skin lesion was dermatofibrosis.

We first examined the patient in October 1964. He denied further episodes. Some residual weakness was evident in the right serratus anterior and both triceps. There was minimal winging of the right scapula. The muscle stretch reflexes were slightly hyperactive but symmetrical. Hemoglobin, white blood cell count, urinalysis, roentgenograms of the chest, and cerebrospinal fluid were reported as normal. The patient was discharged before electromyography could be performed.

The involvement of vocal cord and hemidiaphragm is uncommon. Only 1 case of the latter is known, but this finding is easily overlooked.[9] The patient's recovery pattern is that experienced by the majority of patients.

Case 5. In March 1964, a 56-year-old male epileptic awoke with burning pain over the right shoulder and dorsal aspect of the right thumb. Six hours later he could not elevate the right arm from his side. He was still having pain in the shoulder when he first reported to a physician in May 1964. At this time he was found to have a "frozen" shoulder. This was treated by physical therapy with little success. In August an external manipulation was performed in an attempt to free the shoulder. We first saw the patient the day following manipulation. His shoulder was too painful to allow clinical examination of the muscles. Electromyography revealed numerous fibrillation potentials in the right supraspinatus and infraspinatus muscles and increased insertion potentials in the right triceps. There was a slight reduction in the number of M.U.A.P.s for the strength of contraction in these muscles. Motor conduction was normal in the right ulnar and median nerves. Because fibrillation potentials do not appear until several days following nerve injury, their presence could not be ascribed to the manipulation.

The patient has been seen frequently in clinic for management of his seizures. Laboratory studies of blood and urine, as well as roentgenograms of chest and head, have been normal.

The patient was seen by us again in November 1964. There was some residual weakness of the external rotators and abductors of the right shoulder. Reflexes were symmetrical and normal. The electromyogram was now normal. The brachial plexuses were stimulated in the supraclavicular fossa and the response of the unilateral supraspinatus muscle was recorded by needle electrode. The conduction latencies were equal bilaterally and considered normal.

Case 6. In 1956 a 27-year-old male was admitted to another hospital because of atrophy of the left pectoralis muscle which had begun nine months previously. He said that when he attempted to lift objects with his left arm, the shoulder seemed to "go out of joint." There was no statement in the history regarding pain or sensory function. The examination report described a tall, thin man whose muscles were slender but strong, except for selective atrophy and weakness of the left pectoralis muscle. The muscle stretch reflexes were considered normal.

The electromyogram was reported as normal. The report of a muscle biopsy from the left pectoralis muscle described atrophic changes which were thought to be the result of nerve damage. Hemoglobin, white blood cell count, urinalysis, basal metabolic rate, fasting blood sugar, protein bound iodine, and roentgenograms of the chest were reported as normal.

We first saw the patient in January 1965, when he was hospitalized because of low back pain. Examination of muscle strength was normal except for moderate weakness and atrophy of the left pectoralis and left trapezius muscles. The biceps, triceps, and brachioradialis muscle stretch reflexes were slightly decreased but equal bilaterally. No abnormalities of the sensory system were found.

Motor conduction velocity was normal in the left median and both ulnar nerves. With 1 exception the needle electrode examination of the muscles of shoulder girdle, including left pectoralis and left trapezius, was normal. In one area of the left deltoid muscle there were numerous fibrillation potentials. No M.U.A.P.s were seen. The skin of this area was red and elevated. The patient stated that it had been the site of frequent injections over the past three weeks.

This patient is somewhat unusual because there is no history of pain. However, it is possible that the supervening nine years have erased memory of the details at onset. This case also illustrates a type of muscle injury which can lead to false interpretation of the electromyogram.

Case 7. In January 1965, a 19-year-old girl awoke with a stabbing pain in the left shoulder which radiated to the point of insertion of the deltoid muscle. The pain was constant and unchanging in intensity for three days and then increased in severity the following three days. It diminished subsequently until she was free from pain by the tenth day. On the third day she discovered that it was difficult to lift small children. This was attributed to pain until the seventh day, when she could not elevate the arm against gravity. She did not consult a physician until required to undergo an employment examination in April 1965. At this time she related the above history. There had been minimal improvement over the last month.

A muscle examination in April 1965, revealed weakness in the left deltoid muscle and in the external rotators of the shoulder. The neurological examination was otherwise normal.

Electromyography demonstrated fibrillation in the left supraspinatus and the anterior portion of the left deltoid muscles, with absence of M.U.A.P.s for the latter. There was a decrease in the number of M.U.A.P.s for the strength of contraction in left supraspinatus and infraspinatus muscles. Motor conduction velocity was normal in the left ulnar and left median nerves.

Hemoglobin, white blood cell count, urinalysis, cerebrospinal fluid examination, and roentgenograms of the chest were normal.

The patient stated that four years previously she had awakened with similar pain in the left shoulder which had remained approximately ten days. On that occasion the pain was less severe and paresis did not develop.

This patient is the only female thus far seen with this syndrome. However, she does demonstrate what might be called a typical case.

CLINICAL ASPECTS

Age and sex. The ages of our patients range from 19 to 56 years. Five of the 7 were in the third and fourth decades. Other authors have shown similar age distributions. Six of our 7 patients were males. The early reports of this syndrome were of military personnel, all of whom were males. Later studies of civilian populations have now established that females are also affected but less frequently than males.

Pain. The 2 principal features which bind these cases into a clinical syndrome are the sudden onset of severe pain in the shoulder and occurrence of paresis a few days later. A distracting factor is the wide variation of innervation of the muscles involved, although most commonly they are innervated by the C5 or C6 cord segments.

The pain is severe and burning in character. Most patients use analgesics for relief of discomfort. The initial pain is in the shoulder. It then radiates to the deltoid area or less frequently to the scapula, neck, or arm. Most patients hold the shoulder rigid because movement increases their discomfort. The immobilization can result in the complication of "frozen" shoulder. Neck motion does not increase the pain.

Sensory loss, if it occurs, is usually in the skin area innervated by the axillary nerve.

In Case 1 the pain was first realized when awakening from sleep on 3 separate occurrences. A total of 5 patients said that they had awakened with pain. The remaining 2 could not recall the events surrounding onset. Our review of previously reported cases revealed that in each instance when the circumstances associated with the first realization of pain were recorded, the patient had just awakened. Thus, of Hook's[10] 8 patients, 5 awoke with pain. Weinstein[11] gave histories for 3 of his 18 patients. Two had awakened with pain. Magee and DeJong[8] detailed 3 histories from their series of 23; of these, 2 awoke with pain. Turner and Parsonage[4] gave 1 history from their large series of 82. This patient first felt pain while he was in bed. There are probably several other patients who awoke with their pain. Our Case 3 illustrates the possibility that this may be overlooked or not recorded. If there is any relationship between posture in bed and damage to the brachial plexus, it may be significant that 48% of Parsonage and Turner's[2] 136 cases and 56% of Spillane's[1] 46 patients were in the hospital at the time of onset. We assume that they were spending increased amounts of time in bed.

Patient 7 always slept with arms extended toward the head of the bed. Patient 4 had been sleeping in an unaccustomed and awkward position. Unfortunately this information is lacking for the remaining patients.

It is quite possible that trauma resulting from compression of nerve or vascular structures could be the common etiologic factor in these cases. Minimal trauma could lead to transient or minor symptoms, as in Cases 1, 3, and 7. Severe compression may be expected to result in increased disability. Repeated trauma to injured structures could explain the variable delay period of accompanying paresis. In none of our patients could a toxic exposure by injection or otherwise, be elicited.

Paresis. A few hours to several days after onset of pain, paresis appears on the same side. If pain is bilateral, paresis may occur on one or both sides and affect the same or different muscle groups. The onset of weakness goes unnoticed in some patients because pain discourages movement of the arm.

In all reported series, the deltoid, spinati, and serratus magnus have been the most commonly affected muscles, either alone or in combinations. However, most muscles of the shoulder and upper extremities have been reported as being involved in individual patients. Turner and Parsonage[4] wrote of cases having radial nerve lesions at various levels, or lesions of the anterior interosseus branch of the median nerve concomitant with the more typical syndrome in the contralateral extremity.

Prognosis. It was believed early that prognosis for recovery was poor. Hook,[10] and later Turner and Parsonage,[4] have revised this concept. As can be seen in our cases, the outlook for almost complete recovery is favorable.

Treatment. No effective treatment is known. If trauma resulting from posture is important etiologically, preventive measures can be devised.

Austin[12] has reported a well documented case of recurrent polyneuropathy which responded satisfactorily to adrenocorticotrophic hormone therapy during 20 episodes of polyneuropathy. Our first patient attributed the abortive nature of his last 3 episodes to the effect of prednisolone. Unfortunately none of our patients were seen during the acute stages when a trial of steroids would be expected to have optimum effect.

SUMMARY

Case histories are given of patients who present the syndrome known as paralytic brachial neuritis or neuralgic amyotrophy. The clinical features are reviewed with emphasis on the mode of onset and possible etiology. It is hoped that this report will alert the practitioner to this common neurological disorder.

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Ovulen® as an Oral Contraceptive

EDWARD A. BANNER, M.D.

Rochester, Minnesota

At the time this study was initiated, the ideal of responsible, voluntary parenthood had become an achievable reality to the several million women whose physicians had prescribed oral progestins in a contraceptive regimen. The unprecedented reliability and simplicity of the oral method provided a new freedom from fear of untimely pregnancies and, in addition, improved marital harmony through release from the interference of older mechanical and less reliable methods of contraception. Although no permanent disabling condition has been noted with the use of oral progestins, untoward side effects resulted in the abandonment of the method by some. However, by modification of the chemical structure of the commonly used steroids, new agents became available which made it possible to maintain the same effectiveness and yet, by lowering the total dosage, to reduce to a minimum these occasional untoward effects. It was with this in mind that trials with a combination of ethynodiol diacetate and mestranol (Ovulen®) were begun.

The principle component, ethynodiol diacetate, is a progestin which has been under investigation since 1961. This progestin combined with small amounts of the estrogen, mestranol, closely mimics the effects of the natural ovarian hormones during pregnancy, inhibiting production or release of gonadotropins and thereby suspending ovulation. To what extent other factors, such as alteration of the cervical mucus and endometrial distortion, influence contraceptive efficacy is still a matter of debate.

BACKGROUND

In 1962 Colton and Klimstra[1] reported on the synthesis of norethynodrel which, in combination with a small amount of estrogen, was being marketed as Enovid®. In an attempt to improve on this preparation, a great variety of other synthetic progesterone-like substances were synthesized. It was from these studies that Ovulen® developed. Andrews and Andrews[2–4] reported the increased effectiveness of ethynodrel (in lower dosages than used with norethynodrel) and the marked reduction in side effects. They pointed out the excellent control of menstruation and the elimination of dysmenorrhea. Holmstrom[5,6] reported on the long-term use of Ovulen® and pointed out the possibility of premature ovulation in the first cycle of therapy, which could result in an unplanned pregnancy. He noted that, in general, the number of patients who stopped using Ovulen® because of side effects, such as nausea, was much less than the number who stopped using Enovid®. He did not encounter instances of prolonged amenorrhea.

Tyler[7] described results of long-term studies, in the continental United States, of the prolonged use of progestins combined with estrogen in contraceptive regimens. He noted that with Ovulen® the incidence of side effects was low. In reviewing the world literature, it was his impression that the incidence of side effects, especially nausea, vomiting, headache, and dysmenorrhea as well as chloasma, appeared to be different among various races and under different climatic conditions. Because of the possibility of liver toxicity or adverse metabolic effects, Tyler[7] reported the relevant data of more than 10,000 separate studies of blood chemistry values. These included complete blood cell and platelet counts and determinations of fasting blood sugar, urea, calcium, phosphorus, alkaline phosphatase, cholesterol, lipoproteins, cephalin flocculation, protein-bound iodine, sulfobromophthalein (BSP) retention, serum glutamic-pyruvic transaminase (SGPT), and sedimentation rate. He noted no significant abnormality in patients taking Ovulen®.

Rice-Wray and co-workers,[8] noting the dangers of uncontrolled population growth, sought for an effective, harmless, and inexpensive contraceptive. In a report on their experience in Puerto Rico and Mexico, they noted an increased acceptance of oral contraceptives in these areas compared to the United States. Eighty-five percent of the women in Mexico were considered to

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EDWARD A. BANNER *is with the Section of Obstetrics and Gynecology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.*

be in the very poor or in the lower middle class. The marked decrease in unpleasant side effects may account for the increased acceptance of oral contraceptives. Fertility was not impaired after discontinuance of the medication, and subsequent children were normal. Pincus and coworkers[9,10] studied women in the Caribbean area who were taking progesterone-estrogen combinations cyclically for contraception and noted that the rate of development of suspicious Papanicolaou smears was significantly lower than the rates observed in those using other contraceptive devices. Neither the progress of cervical anaplasia nor cervical carcinoma was significantly affected by the use of these drugs in those under observation.

After an extensive study of Ovulen® in a group of socially deprived women with limited education, Flowers[11] found the drug to be medically effective and acceptable in 93% of the test group. There were no pregnancies among those who took the medication as prescribed. Therapy with Ovulen® began on the day of dismissal from the hospital following childbirth. The women were instructed to resume medication on the first of each calendar month, whether menstrual flow had occurred or whether it was still in progress. Those women who were particularly anxious to nurse their children but who also wanted to use an oral contraceptive were allowed to begin the medication four weeks after delivery. It was thought that suppression of lactation with an oral contraceptive was less of a risk to lactation than was a pregnancy which often ensued in four to six months among these women. In a comparison series of studies,[12–15] the combination of norethynodrel and mestranol provided an acceptable, effective, safe, and reversible method of ovulation control. Furthermore, 84% of the women studied were pregnant within six months after discontinuing the medication. The 78 babies born to these women were normal in all respects.

PRESENT STUDY

The objectives of this study were (1) to determine the efficacy of Ovulen® in the control of ovulation, (2) to ascertain the presence or absence of untoward side effects which might detract from its use for the purpose of contraception, and (3) to determine the patients' acceptance during prolonged use.

One tablet of Ovulen® was given daily for each twenty days beginning on the fifth day after the onset of menstrual flow. It was emphasized that it was important to establish a fixed routine with 1 Ovulen® tablet being taken every twenty-four hours without omission. Although early in the study use of additional means of contraception was suggested during the first seven days of Ovulen® administration in the first treated cycle, this admonition was not given in the latter half of the study. Careful attention was paid to the presence or absence of abnormal gynecologic conditions, such as leiomyomata or endometriosis, by routine physical examinations and appropriate laboratory procedures during the course of the study. Special attention was paid to women who had a history of thromboembolic disease, thrombosis, or thrombophlebitis.

Since the insulin requirement of the diabetic patient occasionally changes when she is taking estrogen, careful attention was paid to those women showing a low renal threshold for sugar or who were known to be diabetic during the course of the study.

Seventy-two women were studied through 805 cycles. The mean age of the group was 28 years (range, 18 to 47) and the mean gravidity at the initiation of the study was 3 (range, 0 to 9).

Since many women taking other progestins had noted weight changes, careful analysis of weight variations from month to month was made (Table 1). Spotting, which ceased when dosage of the medication was increased, occurred in 20 (28%) of 71 women (Table 2) under investigation (1 was lost to follow-up). Only 1 woman reported the development of dysmenorrhea during the course of the study. Chloasma was noted in 1 woman, and edema

TABLE 1

SUMMARY OF WEIGHT CHANGES IN WOMEN TAKING OVULEN®

Change (lb.)	*No. gaining*	*No. losing*
0	9	
1	4	2
2	8	3
3	8	4
4	3	2
5	6	5
6	1	2
7	2	1
8	2	3
9	0	0
10	2	0
11	1	1
12	0	1
15	0	1
18	0	1
Average change	4 lb.	6 lb.
Total	37	26

caused another to discontinue the medication (the medication was discontinued at the patient's request rather than at the physician's). There was no change in the insulin requirement in 3 known diabetics.

During the course of the medication, menstrual bleeding was reported as slight by 30 women, moderate by 39, and heavy by 1 (Table 3). No observation was recorded for 2. The changes from previous average flow were: no change, 29 (41%); change from moderate to slight, 20 (28%); change from slight to moderate, 7 (10%); change from heavy to moderate, 7 (10%); change from heavy to slight, 6 (9%); and change from moderate to heavy, 1 (1%).

After discontinuance of the medication, pregnancy ensued on the average of within three months.

COMMENT

The untoward reactions attributable to the administration of Ovulen® are less frequent and milder than they are with other progestins with which I am familiar. When nausea occurred, it was generally slight and limited to a few days during the first cycle. It was generally less or disappeared completely when the patient took the Ovulen® tablet with her evening meal or with a glass of milk. No antinausea preparations were used during this study. Only 1 patient complained of nausea after the first treated cycle, and no patient complained of vomiting.

During Ovulen® therapy, the menstrual flow changed in about half of the women studied. When changes occurred, the majority noted a decrease in total menstrual flow. The spotting which was noted usually took the form of a slight amount of brownish secretion, which rarely required the use of a sanitary pad. In each case, it ceased when the dosage was doubled and suitable reassurance was given. Amenorrhea was not noted in this series.

Edema resulting from sodium retention was sometimes encountered and satisfactorily treated by salt restriction or controlled by use of a diuretic. As noted from the weight variations, it is difficult to predict, from cycle to cycle, the presence or absence of sodium retention as a cause of weight gain. In any case, the weight gain usually was that which previously occurred premenstrually. Only occasionally, with increase in weight due to salt retention, was the syndrome of premenstrual tension elicited, and in most cases the increase in weight was thought to be due to a real increase in the tissue mass of the body since increased weight was noted following vacations and certain holidays. It was necessary to advise a modified diet when these circumstances were noted.

TABLE 2

COMPLICATIONS IN 71 WOMEN TAKING OVULEN®

Complication	*No.*	*Percent*
Spotting	20	28
Dysmenorrhea	1	1
Edema	1	1
Chloasma	1	1
Change in insulin requirement	0	—

TABLE 3

CHARACTERISTICS OF MENSTRUAL FLOW IN WOMEN TAKING OVULEN®

	No.	*Percent*
Average flow		
Slight	30	42
Moderate	39	54
Heavy	1	1
Unknown	2	3
Change from previous average flow		
No change	29	41
Moderate to slight	20	29
Slight to moderate	7	10
Heavy to moderate	7	10
Heavy to slight	6	9
Moderate to heavy	1	1

Chloasma may be noted occasionally, particularly in brunet women. The degree of pigmentation usually remains constant throughout the course of the medication.

SUMMARY

Daily ingestion of a combination of 1 mg. of ethynodial diacetate and 0.1 mg. of mestranol (Ovulen®) for twenty days of each menstrual period provides fertility control with confidence and affords a high degree of patient acceptance. This regimen has few side effects and its simplicity will make it most acceptable to the patient and to the physician.

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Open (Retropubic) Prostatectomy and Simultaneous Intrapelvic Hernial Repair

LEANDER W. RIBA, M.D., F.A.C.S.,
W. HARRISON MEHN, M.D., F.A.C.S.,
DONALD LOGAN, M.D., and KENT F. BORKOVEC, M.D.

Chicago

VON STOCKUM SUCCESSFULLY OPERATED upon 2 patients, in 1908, by a retropubic extravesical method. He stated that anatomically this approach was less traumatic than the accepted perineal technique. His 2 case reports were published in 1909.[1] The retropubic operation was revived by Millin in 1945.[2] He found the procedure safe and practical and reported 85 cases with 4 fatalities. There have been many publications in the medical literature during the past twenty years favoring the retropubic operation.[3–11]

We have been interested in the extravesical approach since 1949 and reported on our first 14 retropubic patients with 5 intrapelvic hernial repairs in 1951.[9] We have now operated upon 217 patients of which 30 had simultaneous successful hernial repairs. There were 6 bilateral hernial repairs, making a total of 36 hernioplasties. The fifteen-year experience teaches us that the retropubic approach is a direct, simple, and effective method for removing all of the obstructive tissue under vision. Our technique has been improved; the early complications are now prevented and the results better.

In this paper, the radical retropubic operation for carcinoma has not been included. We are, however, very enthusiastic about the pelvic approach over the perineal in these radical operations. Anatomically, the retropubic approach exposed the entire pelvis. In obesity, the Cherney incision will facilitate the entire operation (Figs. 1 and 2).[12,13]

Two hundred seventeen retropubic cases are being reviewed and presented (1950 to 1964). During this period we carried out 357 transurethral prostatic resections. The ages varied between 44 and 87, with an average of 65. Over one-half of our patients manifested hypersensitive or arteriosclerotic vascular disease, 15 had previous myocardial infarctions, and 14 had diabetes mellitus. Coexisting hernias were noted in 30 patients, with 36 hernial repairs.

INDICATIONS

Our indications for open prostatectomy are liberal. Unless contraindicated, any adenomas of 25 gm. or more may be removed retropubically and the smaller glands and contractures reserved for transurethral surgery. An associated inguinal or femoral hernia or a small urethra and any bladder tumors or stones weigh in favor of the open approach. A strictured urethra is best treated by an electrourethrotomy (Riba urethrotome) before or following the prostatectomy.

The morbidity and mortality percentages have been lowered in all types of prostatic operations. The postoperative complications are similar, but the residuals vary. More patients will have urethral strictures and incomplete adenomanectomy following transurethral surgery than by the open suprapubic and retropubic method. Impotency and urinary incontinence are seen oftener following the perineal approach. Sarnoff,[14] in 1931, recommended a vasectomy through a cystotomy incision. Epididymitis can be prevented by routine vasectomies, either scrotal or intrapelvic. With the exception of the perineal operation, the sex function is usually not disturbed. Loss of external ejaculation during inter-

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LEANDER W. RIBA *is associate professor, Department of Urology, Northwestern University Medical School, Evanston, Illinois;* W. HARRISON MEHN, *is assistant professor, Department of Surgery, Passavant Memorial Hospital, Chicago;* DONALD LOGAN *is a fellow in Urology, Veterans Research Hospital, Chicago; and* KENT F. BORKOVEC *is a resident in Urology, Cook County Hospital, Chicago.*

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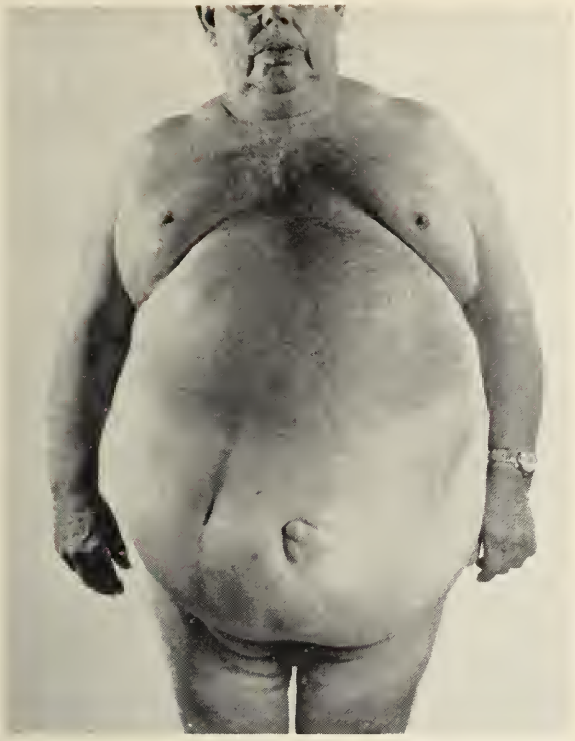

Fig. 1. Acute urinary retention due to enlarged prostate. Patient weighed 325 lb. Cherney incision used to avoid large umbilical hernia

course results from the severing of the ejaculatory ducts incidental to the removal of the adenoma (Fig. 3).

PREPARATION OF THE PATIENT

The patients have a careful history and physical examination. X-rays, including pyelograms, cystograms, and chest films are taken. Blood chemistries, including the phosphatases, blood count and differential, bleeding and coagulation, and prothrombin time and sedimentation rate are recorded. All patients have an electrocardiogram and complete urine studies. If abnormalities are found, a medical consultation is obtained. In the presence of urinary infection a culture is taken and sensitivity tests and preoperative antibiotics are administered. Postoperative antibiotics, parenterally and orally, or both, are routine.

BLOOD LOSS

Hemorrhage is still the major hazard associated with prostatic surgery. Any history of previous bleeding, even though the present blood studies are normal, should be regarded seriously. Operative and postoperative bleeding can be reduced with the following precautions: [1] estrogen substances, intravenous or intramuscular, [2] oxalic acid (Koagamin®) intravenously or intramuscularly, [3] vitamin K (AquaMEPHYTON®) when prothrombin time is low, [4] local hypothermia, [5] aminocaproic acid (Amicar®), 5 to 15 gm. intravenously during and after surgery, and [6] topical agents such as oxidized regenerated cellulose (Surgicel®). The above agents may be safely utilized as an aid in the hemostasis during and after surgery, but their routine effectiveness may not be obvious at all times.

TECHNIQUE

Retropubic surgery of the prostate is carried out under spinal anesthesia, an elevated pelvis in

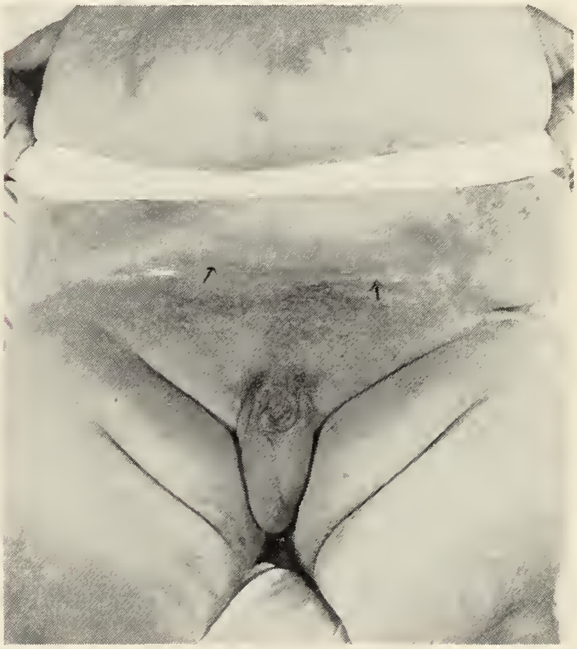

Fig. 2. Postoperative, well-healed scar, Cherney incision

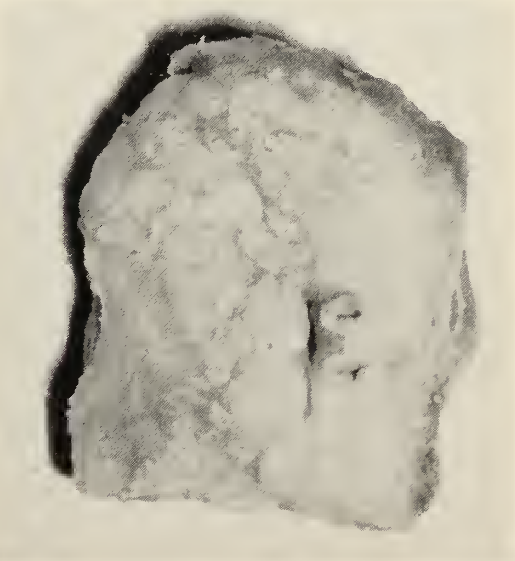

Fig. 3. Gross specimen of prostatic tissue with contained ejaculatory ducts resulting in loss of external ejaculation

the Trendelenburg position is maintained, and an adequate transverse or vertical incision is made (Fig. 4). Dividing the recti tendinous insertions from the symphysis and pubic rami allows the best pelvic exposure. The space of Retzius is entered and all precapsular veins and fat are removed from the prostatic capsule. Three incisions are used to remove the adenoma: [1] transverse capsule, [2] Y incision of the capsule and anterior bladder wall, and [3] vertical vesicocapsular incision involving the proximal capsule (Fig. 5), vesical neck, and anterior bladder wall. After the vesical neck is exposed, the mucous membrane around the internal orifice is incised with a cutting current (Fig. 6), and the adenoma is removed with sharp and blunt dissection under vision (Fig. 7). The urethra is cut with the scissors. After removal, the capsule is palpated. When all obstructive tissue has been removed the empty capsule has a soft velvety feel. Palpable tags are now removed and any bleeders are electrocoagulated or ligated, or both (Fig. 8). When the posterior vesical lip is thickened it should be treated with a V excision. The trigone is sutured to the prostatic capsule with one 00 chromic suture. This obliterates raw surfaces and helps control subcervical bleeding. The incision is closed carefully in two layers, the first continuous and the second interrupted with 00 chromic catgut (Fig. 9). Precision closure prevents postoperative leakage. Recently, we have begun to close the vertical vesicocapsular incision transversely, endeavoring to enlarge the vesical neck. A 24 F. Foley-Alcock catheter is inserted and the wound closed in layers. When the space of Retzius remains dry during wound closure, a suprapubic drain is unnecessary. The catheter is removed in four to five days when urine is clear. When shreds and pus persist in the postoperative urine, urethral calibration may reveal coarctations.

INTRAPELVIC HERNIAL REPAIR

Repair of a unilateral or bilateral hernia is accomplished after prostatectomy and closure of the bladder. The repair is based on the anatomical studies of McVay and Anson.[15] A direct, an indirect, or a femoral hernia may be repaired intrapelvically. The transversalis fascia is sutured with 00 interrupted silk to the superior pubic (Cooper's) ligament medial to the iliac vein. When a large scrotal sac is irreducible, the neck is severed, the contents are reduced, and the peritoneum is closed (Fig. 10). The incarcerated sac may be left in situ. The intrapelvic inguinal ring is then narrowed with interrupted silk sutures. The insertion of the finger tip acts as a guide. In a few cases, one or more sutures need to be placed lateral to the pelvic vessels. Hernial repair requires little or no dissection and has added no known morbidity or mortality. Four additional preperitoneal hernioplasties have been simultaneously carried out with the following urological operations: cystotomy, 2; vesical diverticulectomy, 1; and bladder neck Y plasty, 1.

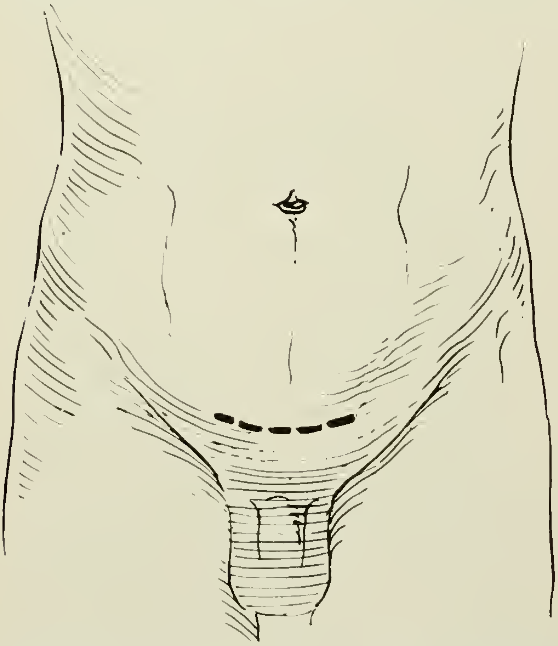

Fig. 4. Transverse skin incision 3 cm. above symphysis including rectus fascia

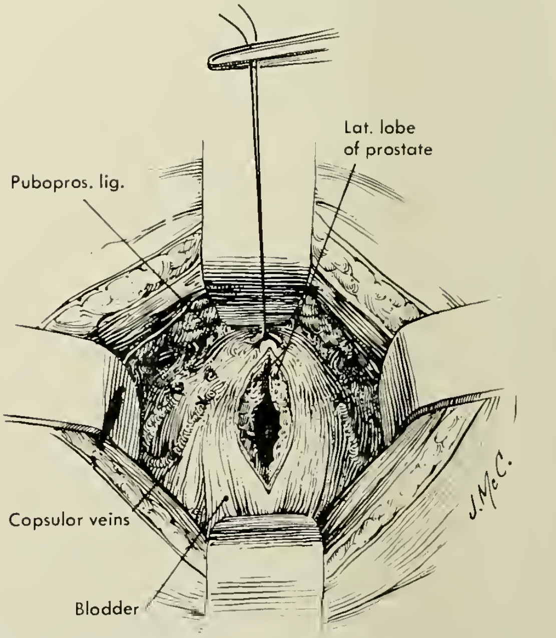

Fig. 5. A vesicocapsular electrosurgical incision through prostatic capsule, vesical neck, and anterior bladder wall

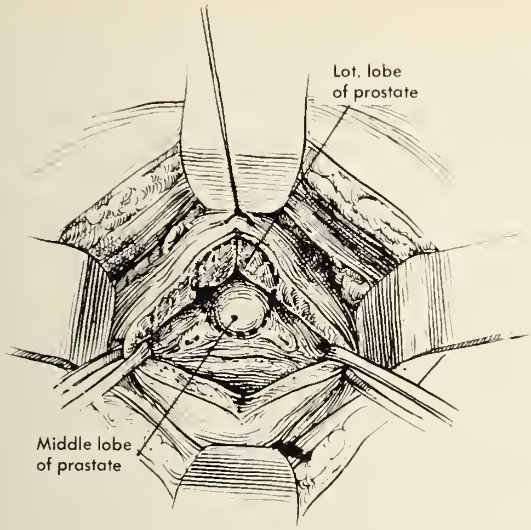

Fig. 6. Trilobular prostate exposed. Dotted line shows circumferential electrosurgical mucosal incision.

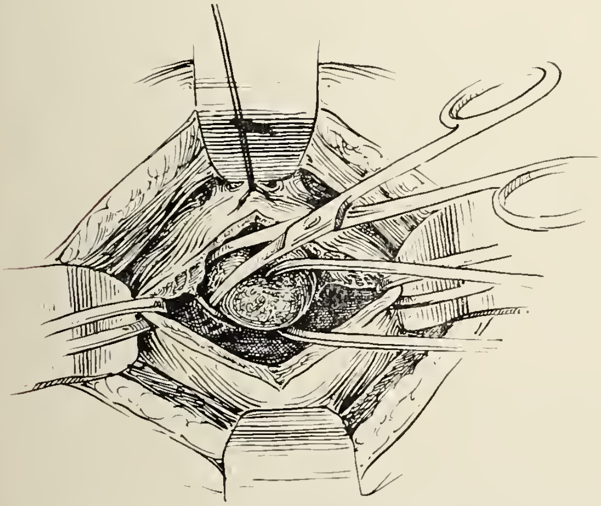

Fig. 7. Sharp scissors dissection of adenoma including transection of urethra

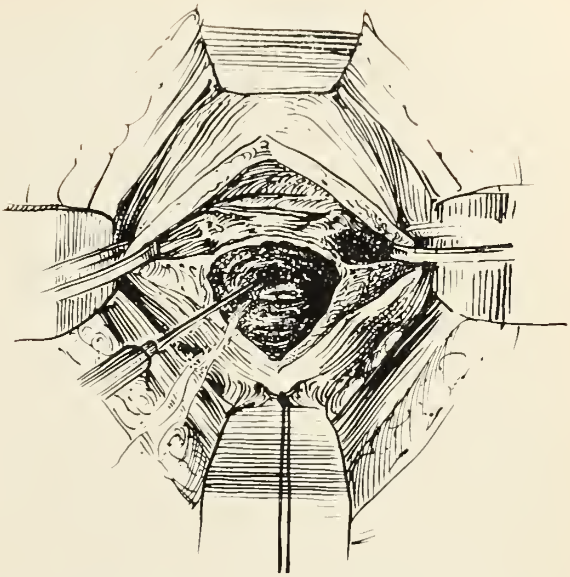

Fig. 8. Empty prostatic capsule exposed. Bleeders ligated or electrocoagulated

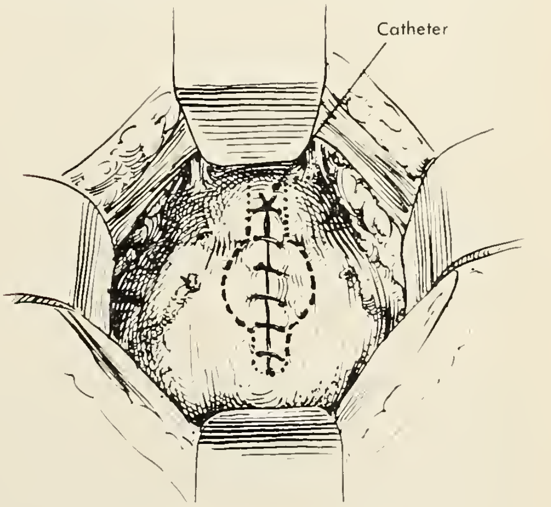

Fig. 9. Vesicocapsular incision is closed in 2 layers. Vertical incision may be closed transversely.

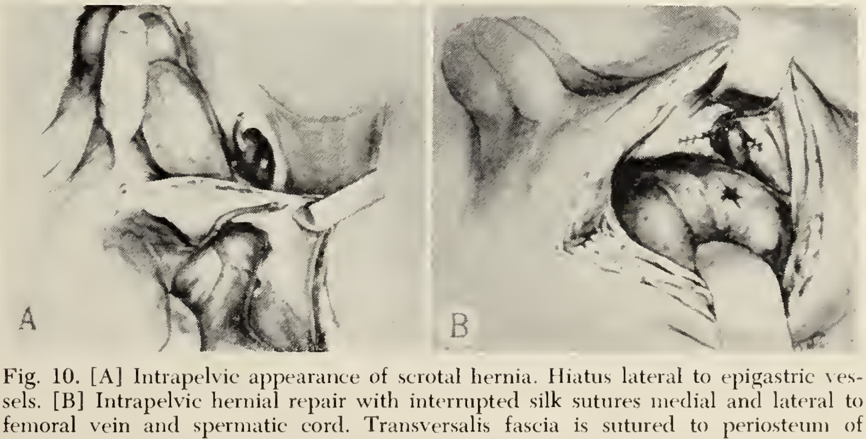

Fig. 10. [A] Intrapelvic appearance of scrotal hernia. Hiatus lateral to epigastric vessels. [B] Intrapelvic hernial repair with interrupted silk sutures medial and lateral to femoral vein and spermatic cord. Transversalis fascia is sutured to periosteum of pubic ramus. Peritoneal opening closed with purse-string suture

Combined open prostatectomy and herniorrhaphy have previously been recommended by others. MacDonald and Huggins, in 1949, advocated suprapubic prostatectomy and simultaneous external incision hernial repair. Moore (1952)[16] and Jaspers (1963)[7] recommended a subcutaneous, external, modified Bazzini hernial repair and prostatectomy as a single procedure by utilizing an extension of the transverse (Pfannenstiel) incision to the inguinal area. I believe, according to all available records, we at Northwestern University Medical School Center have priority on the combined procedure of open prostatectomy and simultaneous preperitoneal hernial repair.

Intrapelvic hernia repair is a controversial field of surgery. It rubs shoulders with general surgery. However, it is a field where cooperation between the general and urologic surgeon can accomplish increased benefits to the patient. This technique is in no way intended to replace the conventional herniorrhaphies. When the lower abdomen is opened for a surgical procedure and a hernia is present, simultaneous repair can be considered.

RESULTS

The results in 217 cases have been satisfactory. There were 5 postoperative deaths (2.3%). One occurred on the fifth postoperative day and another on the night following surgery, both from myocardial infarctions. One diabetic patient died sixteen days postoperatively due to myocardial failure. Two patients succumbed from renal failure, six and twenty-eight days postoperatively. The average hospitalization was fifteen days. Transfusions averaged 1.2 units per patient. Twenty-four percent of the patients received no blood. Six of the first 50 patients required cystostomy for bleeding, but none after that. The average weight of the adenoma was 48 gm. Sixteen tumors weighed over 100 gm., and 32 weighed less than 20 gm. Microscopic sections revealed prostatic hyperplasia in all tissue sections, with evidence of infection in 40%. Unsuspected carcinoma was noted in 13 of the microscopic slides. Associated bladder calculi were removed in 7 patients. Bladder diverticula were present in 11, but only 1 was removed because the other 10 seemed to be nonretentive. Thirty patients underwent intrapelvic hernial repairs (36 hernioplasties) with no increased morbidity. Three repaired hernias recurred (8.3%). One of these failures had been repaired with catgut.

The reason for this paper is to evaluate our results following prostatectomy. We wish to emphasize visual sharp and blunt dissection in removing the adenoma. Blind avulsion prostatectomy is unsurgical and obsolete and should be discontinued. The morbidity (fifteen days) and mortality (2.3%) are low, and the end results are satisfactory. There have been 28 late recurrences (seventeen days to four years, average

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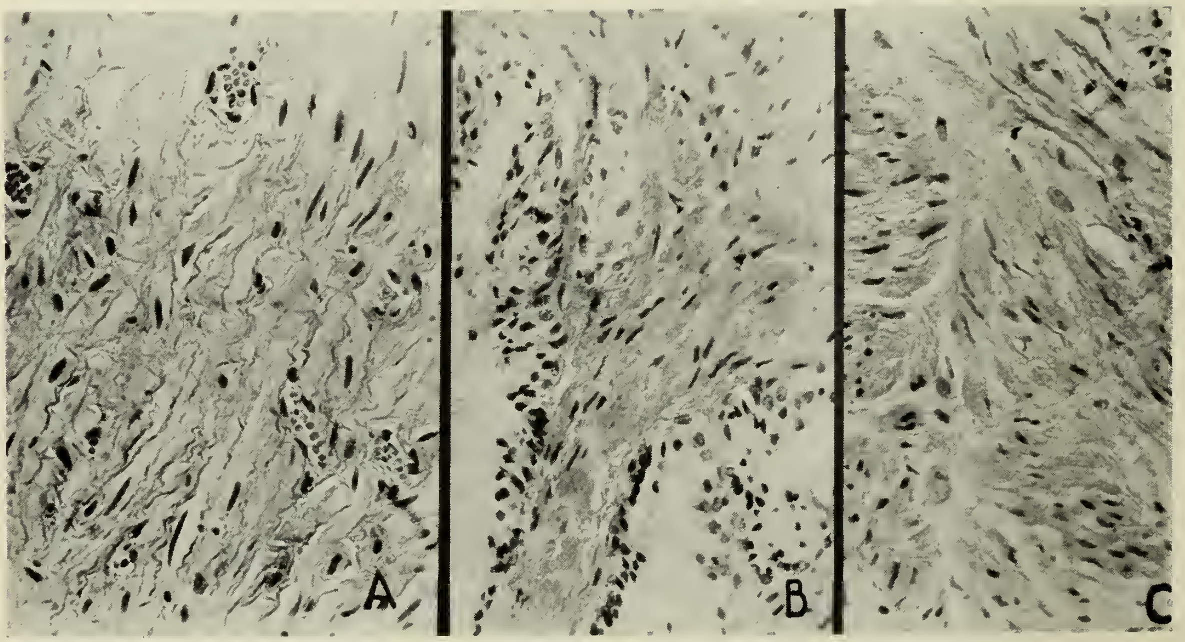

Fig. 11. Microscopic sections of tissue removed transurethrally for late bladder neck obstruction. [A] fibrosis, [B] recurrent hyperplasia, [C] muscular hypertrophy

Transactions of the North Dakota State Medical Association

SEVENTY-NINTH ANNUAL MEETING

Fargo, North Dakota, April 29, 30 and May 1, 1966

(Continued from the August 1966 issue)

PROCEEDINGS

House of Delegates, Second Session

Fargo, North Dakota, May 1, 1966

Speaker Christoferson called the meeting to order at 1:00 P.M. at the Town House Motel at Fargo, N.D.

Dr. Richard S. Larson, Chairman of the Credentials Committee, reported there was a quorum present.

Secretary Buckingham called the roll and the following delegates responded:

Drs. H. A. Norum, Fargo; M. H. Poindexter, Fargo; A. C. Burt, Fargo; Roy Kulland, West Fargo; Paul Beithon, Wahpeton; B. F. Amidon, Fargo; R. J. Ulmer, Fargo; G. H. Hilts, Cando; R. D. McBane, Devils Lake; C. R. Miller, Bottineau; J. A. Sandmeyer, Grand Forks; G. L. Countryman, Grafton; R. H. Leigh, Grand Forks; K. S. Helenbolt, Grand Forks; H. W. Evans, Grand Forks; W. T. Powers, Grand Forks; L. A. Giltner, Minot; R. S. Larson, Velva; Brian Briggs, Minot; A. M. Cameron, Minot; C. J. Klein, Alternate, Valley City; J. J. Moses, Bismarck; M. A. K. Lommen, Bismarck; R. J. Dunnigan, Bismarck; P. O. Dahl, Bismarck; E. G. Vinje, Hazen; E. H. Boerth, Alternate, Bismarck; E. O. Hieb, Jamestown; J. V. Miles, Jamestown; D. E. Skjei, Williston; W. C. Hanewald, Dickinson; R. E. Hankins, Mott; J. M. Little, Mayville.

There were 33 delegates attending the Second Session.

Others present were:

Drs. Nierling, Dodds, Glaspel, McLean, Pederson, Painter, Naegeli, Peters, Christianson, Fox, Van Der Linde, Toomey, Mr. Limond and Mr. J. Sherwood Williams.

SECRETARY BUCKINGHAM: Telegram received—to Dr. J. D. Craven, President: "Best wishes for a very successful convention. Signed, Rolland Redlin, Congressman, West District." and To—President of North Dakota State Medical Association: "The City of Minot and the Parker Hotels cordially extend an invitation to your Convention Body and its Board of Directors to consider Minot and the Parker Hotels as the site for your 1967 Convention. We pledge our complete cooperation. Best wishes for a successful meeting in Fargo. Signed, Lyle Smith, General Manager, C. P. Hotel."

A motion was made by Dr. Ulmer, seconded by Dr. Klein, that the reading of the minutes of the first session be dispensed with. Motion passed.

SPEAKER CHRISTOFERSON: It is a privilege to recognize our members who have practiced in their chosen profession of medicine for fifty years or more, and to reward them for their unselfish devotion to their patients, and for their loyalty to the medical profession. We are very privileged to have two of them present today. I would like to read the data about these physicians, and then I would like our President-Elect, Dr. Toomey, to present these Certificates and 50-Year Pins to these doctors.

Dr. Charles R. Tompkins of Grafton, N.D. was born April 4, 1889 in Benson County, near Oberon, North Dakota. He was graduated from Rush Medical College in 1916, and was licensed to practice in North Dakota in 1918. He practiced at Oberon until 1926 when he moved to Grafton, and has practiced there since that time. He became a member of the Association in 1924. He is a General Practitioner and General Surgeon.

(Mr. Limond assisted Dr. Tompkins to the rostrum.)

DR. TOOMEY: It is a pleasure and an honor to present you this token of recognition for your 50 years of service to the people in your community. I hope you will be around for the 75th.

DR. TOMPKINS: Thank you very much.

SPEAKER: The next gentleman here this afternoon is Dr. Max T. Lampert from Minot. Dr. Lampert is in private practice. He was born in 1895 in Chicago; was graduated from the University of Illinois, Chicago, in 1916. He practiced in Chicago before coming to North Dakota in 1935. He has been a member of the North Dakota State Medical Association since that time. He is a life member of the American College of Surgeons, the American Academy of Ophthalmology and Otorhinolaryngology, and the Minnesota Academy of Opthalmology and Otorhinolaryngology.

(Mr. Limond escorted Dr. Lampert to the rostrum.)

DR. TOOMEY: It is a pleasure, Dr. Lampert, to greet you here, and also a pleasure to know that you are working every day. It is an honor and a privilege to present these tokens of recognition of your unselfish devotion to your patients and of your loyalty to the Medical Profession.

DR. LAMPERT: Thank you very much.

(The speaker read the data about the other 50-year members who could not attend the meeting. Certificates of Distinction and 50-Year Pins will be sent to them.)

Dr. Adam F. Panek of Milton, N.D. Born December 23, 1885 in Traverse City, Michigan, was graduated from Chicago College of Medicine and Surgery in 1916. Following graduation, practiced at South Bend, Indiana. Served in the U.S. Army during World War I. He was licensed in North Dakota in 1920, and has resided and practiced at Milton since that time. He became a member of the North Dakota State Medical Association in 1924.

Dr. Paul H. Rowe, Northwest Clinic, Minot, N.D. Born July 24, 1892 at Casselton, N.D.; was graduated from Rush Medical College in 1916; licensed in North Dakota in July, 1928. Prior to that time he practiced in Chicago, Illinois, and Minneapolis, Minn. He has been a member of the North Dakota State Medical Association since 1929. His specialty is Internal Medicine.

Dr. Angus L. Cameron, Northwest Clinic, Minot, N.D.

Born February 10, 1891, in Hamilton, Indiana. He was graduated from Rush Medical College in 1916, and licensed in North Dakota in January, 1925. He has been a member of the State Association since date of licensure. His specialty is General Surgeon.

(A motion was duly passed that a letter, signed by the President, be sent to the physicians named above.)

Dr. F. D. Naegeli next reported for the Board of Medical Examiners. His report follows:

"As Chairman of the Board of Medical Examiners, I thought you might be interested in a brief report of the work done in 1965.

There were 47 applications for medical licenses during 1965; 17 applied for licensure by examination. Of these, one failed; two were U.S. citizens and were awarded permanent licenses; 14 of the 17 were non-citizens, passed the examination and were issued temporary licenses which can be replaced by permanent licenses when U.S. citizenship is obtained. The 17 applicants were: 6 from Canada; 2 each from the British Isles, Dominican Republic, and the Philippines; 1 each from Greece, India and Iran.

Thirty candidates were licensed by reciprocity. Of these, in ten instances, licensure was based on National Board Certificates; four each from Minnesota and Ohio; three from Wisconsin; two from Texas, and one each from Michigan, North Carolina, South Carolina, South Dakota, Nebraska, Pennsylvania and Missouri.

I thought you would be interested in a little information concerning the number of these indivduals who still remain in North Dakota. Of the 46 individuals who were given temporary or permanent licenses, two are still in residencies; 4 never took up residence in North Dakota; 10 practiced for a few months and left the state, and 30 still remain in North Dakota actively engaged in the practice of medicine. In other words, the attrition after one year is about one-third.

You might be interested in other activities of the Board. One activity was the investigation carried on by Drs. Cleary and Nuessle concerning a Medical-Osteopathy Composite Board of Medical Examiners, and the other was filing a complaint against Mrs. Iola Gifford of Flasher, N.D. for violation of the Medical Practice Act. The latter complaint is still in the courts, and you will doubtless hear more about this."

Dr. Larson moved that the report be adopted. Seconded by Dr. Vinje and passed.

Mrs. M. A. K. Lommen, President, Woman's Auxiliary, was introduced by the Speaker for the purpose of addressing the House on the activities of the Woman's group.

PRESIDENT'S ADDRESS, WOMAN'S AUXILIARY

It is my purpose to tell you of the activities of the twentieth year of the Woman's Auxiliary to the North Dakota State Medical Association. We are a segment of the National Auxiliary, as you are of the American Medical Association.

Our National membership was 88,301; our State membership is 345. Yours is 437.

The Medical Auxiliary Student Loan Fund in its 16th year, has, through memorials and contributions, increased by $2,620.00, bringing the total to $34,720.45. Add interest earned at 2½% in the past year—the total value is $34,985.66. Approximately $70,000.00 in loans has been granted by this revolving fund. A total of 137 loans has been granted.

Our gifts to AMA–ERF this year, designated to the University of North Dakota Medical School, total $1,442.90. $50.00 has been designated to a second medical school. Total $1,492.90. Your checks—designated to the category of your choice, and made out to AMA–ERF Auxiliary Fund can be credited to our Auxiliary.

We have been saddened by the departure from our pathways of Mrs. Paul Burton, Mrs. Reinhold Goehl, and Mrs. Robert McFadden.

Drug samples, soap, bandages, and hospital gowns are being shipped to World Medical Relief, Detroit, from this convention. This constitutes our International Health Activities.

To the Grand Forks Chapter of Woman's Auxiliary to Student American Medical Association, we have contributed $100.00 to help send their delegate to their National Convention, to be held this year in Los Angeles, California.

Our Health Careers Chairman is busy. There are five Health Careers Clubs in the State. The State Rally was held in September in Minot with 117 present. The next Rally will be held in Bismarck. The North Dakota Health Careers Council has three Auxiliary members on its Board. This Council is now compiling a very complete booklet on Health Careers Opportunities in North Dakota. Five thousand copies are to be published this summer. These young people have demonstrations, tours, medical speakers, and work opportunities in their program.

Our fund raising projects were Medical Balls, rummage sales, and silent auctions.

One District is financially assisting a school for the mentally retarded. A second District pays the tuition for a trainable child. Two Districts are participating in a Suicide Prevention Project, and in two Districts volunteers work in Mental Health facilities.

Our members are a credit to the Auxiliary in their Community Service work. They have worked individually or in groups on parties for senior citizens, health careers, Future Nurse Organizations, Candy Stripers, immunization clinics and school health; on Mental Health programs, United, Heart, and Cancer Funds, P.T.A., Scouting, religious groups, and everything that is going.

One question on our National Legislative Report Form states—'Does your State Medical Society request the assistance of the Auxiliary in legislative work on the state level?' We have an Auxiliary member on the North Dakota state board of COMPACT.

One District helped publicize the need for standards to be set regarding ambulance equipment, drivers, and attendants. The purpose was to stress the need for training, legislation, and the problems involved.

Our Official Publication—News, Views and Cues will be published three times this year. I hope that you read it. The Grand Forks girls are doing a nice job on it. We wish to thank Blue Shield for caring for postal expense on distribution of these issues.

I wish to thank the seven districts we officially visited for their hospitable reception.

May I express my thanks to the Office of Executive Secretary for its excellent cooperation. Mr. Limond, Mrs. Fremming, and Mrs. Kohler, we appreciate your help.

The financial assistance of $200.00 each year from the North Dakota State Medical Association for convention makes our convention possible. We thank you.

I should like to thank my family, especially my husband, for his patience.

Our total budget for the year came to $1,119.00. Our income is through state membership only; state dues are $3.00; and our state membership is 345, the highest number to date. Our total income is then $1,035.00. That rock we had has been chipped away. We have come through the chip size and the pebble size, and are in the sand. I just hope it isn't quicksand. We do not propose that you bail us out. You ask yourself if your wife is a member. What is the very least that she can do?

I'd like to tell you of events following the report of last spring that "100%" team-membership was approved: One District Society tabled the motion; one District stated it could not collect dues for another organization: two District Auxiliaries collected only local dues, awaiting action, which never came, from the District Society. One District solved the problem by enacting "100% team-membership." Surely, this is the most impartial way to handle our membership problem. The States which have enacted "100% team-membership" are:

Idaho, with a membership of	516
Nevada, with a membership of	227
Hawaii, with a membership of	575
Montana, with a membership of	607
New Mexico, with a membership of	590
Utah, with a membership of	645

Only one is smaller than we. So that you can help us to help ourselves, I would like to ask that you implement "100% team-membership." The difference of 92 members can really keep us afloat. For $5.00 that's quite a bargain.

You have every reason to be proud of the work of the members of your Auxiliary. Mrs. Edwin O. Hieb, Jamestown, has been installed as President for 1966-67. She is a most capable and enthusiastic person who will prove to be an excellent presiding officer of the Auxiliary.

I thank you for your time, your interest—and "100% team-membership."

SPEAKER: The House of Delegates in 1965 unanimously passed a motion recommending that the Council approve the billing of dues for the Woman's Auxiliary along with the regular billing of dues for the State Association. It was moved by Dr. Vinje, seconded by Dr. Larson that the 1965 action of the House be brought to the Council for action.

Reference Committee to Consider the Reports of the President, Secretary, Executive Secretary and Treasurer

Dr. Hankins, chairman of this committee, presented the following reports and their discussions, which were adopted section by section, and as a whole.

1. Report of the President. This report was reviewed and approved. The Committee commended the President for a job well done and, in view of the volume of his work, also commended his report on its completeness and brevity. This portion of the report was adopted.

2. Report of the Secretary. This report was reviewed and approved. This portion of the report was adopted.

3. Report of the Executive Secretary. This report was reviewed and approved. The Reference Committee commended Mr. Limond for his continued excellent representation of the Association in his activities, and his good work for the doctors in the state. The Committee noted with approval the excess of receipts over disbursements. This portion of the report was adopted.

4. Report of the Treasurer. This report was reviewed and approved, as audited. This portion of the report was adopted.

The motion was made by Dr. Hankins, seconded by Dr. Powers, that this report as a whole be adopted. Motion carried.

DR. ROBERT E. HANKINS, *Chairman*
DR. R. E. KULLAND, *Vice-Chairman*
DR. C. ROBERT MILLER
DR. WILLIAM T. POWERS
DR. RALPH DUNNIGAN

Reference Committee to Consider the Reports of the Council, Councillors, Special Committees and the Report of the Representative to the Blue Shield Board of Directors

Dr. Countryman, chairman of this committee, presented the following reports and their discussions, which were adopted section by section, and as a whole, with amendments.

1. Report of the Chairman of the Council. The report of the Chairman of the Council was reviewed by the Reference Committee and the following special observations were noted:

(a) We commend Dr. Willard Wright for his untiring efforts in representing this Association with the American Medical Association; (b) This committee is in accord with the $100.00 contribution to the Science Fair; (c) The new format of the State Medical Meeting was successful; (d) The 1967 Annual Meeting was voted to be held in Jamestown, but we note that the Council is in agreement that the Annual Meeting be held in Bismarck in 1967; (e) We commend the Chairman of the Council for a job well done.

This portion of the report was adopted.

2. Reports of the Councillors. The Reference Committee reviewed the reports of the Councillors of all ten districts and commended them for their thoroughness. This portion of the report was adopted.

3. Report of the Committee on Cancer. This report was reviewed and approved. The Reference Committee noted with interest the Cancer Society's intention to provide more literature on cancer in the pediatric age group. It was further noted by the Committee the recent retirement of Mrs. Mary Snyder, longtime Executive Director of the North Dakota Cancer Society. They recommended that the Association Secretary write a letter of commendation and thanks to Mrs. Snyder for her years of faithful service. This portion of the report was adopted. Speaker Christoferson charged the Executive Secretary to draft such a letter to be forwarded to Mrs. Mary Snyder from the North Dakota State Medical Association.

4. Report of the Committee on Nursing Education. This report was reviewed and approved. This portion of the report was adopted.

5. Report of the Committee on Maternal and Child Welfare. This report was reviewed by the Reference Committee, except for the resolution on abortion. It was noted that a second resolution on abortion would be considered by Reference Committee No. 6. Two amendments were made to the original report submitted by the Committee on Maternal and Child Welfare. First, the words "antiseptic solution" were to be substituted wherever the word "phisohex" appears, and second, the House emphasized that nurses be properly trained and given special instructions before being allowed to make pelvic examinations. This portion of the report was adopted, as amended.

6. Report of the Committee on Foreign Trained

Physicians. This report was reviewed and approved. The Committee commended Dr. Glaspel for his endeavors. This portion of the report was adopted.

7. Report of the Committee on Diabetes. This report was reviewed and approved. This portion of the report was adopted.

8. Report of the Committee on Crippled Children. This report was reviewed and accepted by the Reference Committee, with the recomendation that a list of all procedures covered, and their approximate cost, be sent to all physicians in the State, so that minor conditions might be eliminated, and that acceptance or non-acceptance of other conditions might be better made at a county level. It was also recommended that the medical authorities involved be more cognizant of the interest on the part of the referring physician in progress reports. This portion of the report was adopted.

Speaker Christoferson suggested that the best way to handle this might be to have the Chairman of the Committee on Crippled Children prepare the report, and that he supply it to the membership through the Executive Secretary's office.

9. Report of the Committee on Mental Health. This report was reviewed and approved. This portion of the report was adopted.

10. The report of the Liaison Committee to the North Dakota State Bar Association. This report was reviewed and approved. This portion of the report was adopted.

11. Report of the Committee on Pharmacy. This report was reviewed and approved by the Reference Committee with the recommendation that this committee be continued for the ensuing year. This portion of the report was adopted.

12. Report of the Committee on Emergency Medical Service. This report was reviewed and approved. This portion of the report was adopted.

13. Report of the Committee on Liability Insurance. This report was reviewed and approved. This portion of the report was adopted.

14. Report of the Liaison Committee to the North Dakota Dental Association. This report was reviewed and approved. This portion of the report was adopted.

15. Report of the Committee on Cardiovascular Diseases. This report was reviewed and approved. This portion of the report was adopted.

16. Report of the Committee on Medicine and Religion. This report was reviewed and approved. This portion of the report was adopted.

17. Report of the Committee on Aging and Rehabilitation. This report was reviewed and approved by the Reference Committee, who commended Dr. Don Barcome, Director of the Rehabilitation Unit, Grand Forks, and the members of the Committee on Aging and Rehabilitation for their efforts in increasing the utilization of the Medical Rehabilitation Unit, now working near capacity. This portion of the report was adopted.

18. Report of the Medical Advisory Committee to the State Highway Department. This report was reviewed and approved, with the recommendation that this committee continue its work with the Safety Responsibility Division of the State of North Dakota in providing medical advice concerning the licensing or rescinding of licenses to special risk drivers. It was also recommended by the Reference Committee that the possibility of obtaining state legislation, such as the Good Samaritan and Battered Child Laws, be considered to protect physicians who detect and report such special risk cases. The Reference Committee supported the Committee's request for the cooperation of doctors throughout the state. This portion of the report was adopted after the following remarks:

SPEAKER: Is there any discussion? There has been a great deal of interest in this report. We are moving here that the Medical Advisory Committee continue its work in providing medical advice concerning the licensing or rescinding of licenses to special risk drivers.

DR. AMIDON: I think the important part of this is the phrase, "special risk driver," and suggest that there would be some way of channeling this information to the Safety Department so that they can rescind these drivers' licenses.

DR. ULMER: I do not feel we should rely on doctors to report. There should be a regular examining feature on these cases and not have the doctors make a report.

DR. LEIGH: Reference Committee, number three, has an addendum to this report, favoring special examinations.

19. Report of the Committee on Constitution and By-Laws. This report was reviewed and approved by the Reference Committee, with the recommendation that the Committee on Constitution and By-Laws further investigate the feasibility of establishing commissions as a replacement for the present committee system, in each of the following areas: (1) Medical Service (2) Scientific Medicine, (3) Legislation and Governmental Relations, (4) Communications, and (5) Allied organizations. The Reference Committee further recommended a reference committee for each of these areas, in addition to a reference committee on resolutions. This portion of the report was adopted.

20. Report of the Representative to the Blue Shield Board of Directors. This report was reviewed and approved by the Reference Committee, with the recommendation that members study this report to become knowledgeable of decisions now facing North Dakota Blue Shield. The Board of Directors of Blue Shield await action by the House of Delegates as follows:

A. A directive indicating whether reimbursement to participating physicians in North Dakota Blue Shield be made by a revised fee schedule, or totally on the basis of usual and customary fees.

B. Whether North Dakota Blue Shield should continue the philosophy of trying to help low income groups, or abandon this philosophy.

C. Whether North Dakota Blue Shield should provide a major increase in fees to participating physicians, thus requiring a premium increase to the subscriber of almost double the present premiums, or whether modifications in the present fees be made in areas of inequity with only a minor increase in premiums to the subscriber.

D. Implementation of a utilization review committee and of a claims review committee by the North Dakota State Medical Association.

Your reference committee recommends the following:

A. Reaffirmation of the philosophy of trying to help low income groups prepay medical costs on a private basis.

B. Modification of the present fee schedule with respect to such inequities as are indicated by the Committee on Medical Economics, and with a specific recommendation that cost of living changes be reflected in the fee submitted as usual and customary.

C. Recognizing that Plan D of Blue Shield provides for the payment of usual and customary fees, accept a modified version of the present fee schedule and urge negotiations with Medicare be made on the basis of Plan D.

D. Develop a Blue Shield Claims Review Committee from the North Dakota State Medical Association. Members would receive remuneration as provided under Medicare.

A short discussion followed.

DR. LEIGH: On part two of the recommendation, it seems to me that we were told this morning there has not been an increase in Blue Shield for six years. If we are going to have an increase in the remuneration, should not our fees be up-dated now and provision be taken in the future to do this on an annual basis, instead of trying to do this all at once.

DR. CAMERON: Will this be a yearly increase in rates?

SPEAKER: No, I do not believe there would be an increase on a yearly basis. I would anticipate that Blue Shield might budget the rate increase on the basis of the usual and customary fee schedule; and on the basis of the correction of the inequities of the fee schedule as indicated by the Committee on Medical Economics. The Committee on Medical Economics will meet right after this meeting, to come up with some recommendations to Blue Shield so that they can submit these recommendations to the Actuary.

This portion of the report was adopted.

21. Report of the Representative to the Crippled Childrens Services Division of the Public Welfare Board of North Dakota. This report was reviewed and approved. The Reference Committee is in accord with the provision of speech therapy by CCS for all children under seven years of age who are referred by a specialist authorized by the Crippled Childrens Services. It was noted that dental problems resulting from a diagnosis coming within the medical scope of Children Services Program should be included and the provision made for general dentistry in these instances. It was further noted that under CCS the specialist may refer the child back to the family physician or general practitioner for post-operative or follow-up care. This portion of the report was adopted.

The Reference Committee recommended that the President appoint a committee to study the feasibility of establishing a Medical Museum in the state. This portion of the report was adopted.

Dr. Countryman moved that the report be adopted as a whole, with amendments. The motion was seconded by Dr. Norum. Motion carried.

DR. G. L. COUNTRYMAN, *Chairman*
DR. R. D. MCBANE, *Vice-Chairman*
DR. H. A. NORUM
DR. BRIAN E. BRIGGS
DR. B. J. AMIDON

Reference Committee to consider the Reports of the Delegate to the AMA, Medical Center Advisory Council, Committee on Medical Education, and the North Dakota State Advisory Council for Hospital and Related Construction

Dr. Miles, chairman of this committee, presented the following reports and their discussions, which were adopted section by section and as a whole.

1. Report of the North Dakota State Advisory Council for Hospital and Related Construction. This report was reviewed and approved. This portion of the report was adopted.

2. Report of the Representative to the Medical Center Advisory Council. This report was reviewed and approved. This portion of the report was adopted.

3. Report of the Delegate to the American Medical Association. This report was reviewed and, at the request of the Delegate to the AMA, brought the following actions of the AMA House forward for consideration. The actions, and the Reference Committee comments are as follows:

A. The AMA House approved the Board of Trustees' recommendation to increase AMA dues, effective January 1, 1967, from $45.00 to $70.00. This matter will come to a final vote at the AMA Convention in June.

Your reference committee approves of this action.

B. Your reference committee agreed with the action of the AMA House when it adopted the "usual and customary fee" concept as the basis for reimbursing physician participants in governmental programs at all levels, and when it urged the acceptance of this concept upon all third parties.

C. A resolution by the AMA House urges state and county medical societies to participate in public hearings in the development of appropriate standards which would assure uniform signs on our limited access highways and interstate systems indicating the location of the nearest licensed hospital.

Your reference committee sees some merit in this and has no objection to the general intent of this resolution.

D. Your reference committee agrees with the continued effort of the local and state medical societies to provide efficient physician representation on the Hill-Burton Advisory Councils and area-wide planning agencies, and to play an active role in the stimulation and development of voluntary health facility and services planning—to initiate and help formulate community health facilities and service studies in their local areas.

E. The reference committee urges acceptance of the AMA House resolution that medical staffs and state and component medical societies encourage establishment, maintenance, and proper use of cancer registries in hospitals.

F. Your reference committee approves the AMA House resolution that state and local medical societies encourage widespread community development of the Explorer Scout Program for Medical Specialty Posts, throughout the United States.

G. The committee agrees that the State Medical Association should sponsor conferences on utilization to provide guidance for physicians in establishing utilization review and claims review at the local level.

This portion of the report was adopted.

4. Report of the Committee on Medical Education. The Reference Committee noted that there had been no official meeting of the Committee on Medical Education, but that the Speaker had assigned the matter of the Heart Disease, Cancer and Stroke Amendments of 1965 (P.L. 89-239) to be considered. The Reference Committee drew the following conclusions in connection with P.L. 89-239:

A. That, North Dakota is a large area with the only medical school between the Twin Cities and Seattle, and there are already established within the state several facilities offering high-grade medical care in the areas of heart, stroke, and cancer which should be fostered to further better available care;

B. That, postgraduate medical education in the state should be studied carefully with the goal to make it more effective, and to coordinate the programs which are at present diversified and fragmented. (State annual meetings, District Medical Society meetings; A.A.G.P., Colleges of Physicians and Surgeons, Ob-Gyn., etc.);

C. A planning grant would provide personnel and funds to make a careful evaluation of our existing resources, communication problems, patient referral, postgraduate education, hospital facilities, diagnostic centers and treatment centers; and,

D. Definitive medical care as it has evolved, involves complex, expensive apparatus and highly trained personnel. Further, it requires a volume of patients to warrant the installation and operation of such apparatus and the effective use of such personnel;

E. Even though facilities have developed in a reasonably efficient way in North Dakota and neighboring states, pooling of resources and state-wide support must be planned cooperatively in the best interests of the patient, consequently,

   1. This reference committee feels that the application should be made for a feasibility study considering North Dakota, including western Minnesota, northern South Dakota, and eastern Montana, as an economic, socially related, functionally coherent geographic area under the terms of P.L. 89-239;
   2. We feel strongly that the leadership should be provided by the North Dakota State Medical Association and its officers;
   3. Your reference committee recommends that if this study brings to light a need for such a program, the North Dakota State Medical Association review and re-evaluate and approve the program before application is made for an operational grant;
   4. We further recommend that the North Dakota State Medical Association create a Foundation for the purpose of applying for the feasibility grant, inviting all concerned parties to participate in this study.

This portion of the report was adopted, after an amendment to include practicing physicians on any committee which may conduct a feasibility study.

Dr. Miles moved that the report, as amended, be adopted as a whole. The motion was seconded by Dr. Dahl and carried.

Dr. James V. Miles, Jr., *Chairman*
Dr. Robert J. Ulmer, *Vice-Chairman*
Dr. Harold W. Evans
Dr. A. Malcolm Cameron
Dr. E. H. Boerth, *Alternate*

Reference Committee to Consider the Reports of the Standing Committees, except Committee on Medical Education and Committee on Medical Economics

Dr. Little, chairman of this committee, presented the following reports and their discussions, which were adopted section by section and as a whole, as amended.

1. Report of the Committee on Necrology and Medical History. The Reference Committee reviewed and approved this report and commended Dr. Boerth for his fine efforts as Chairman of this Committee. This portion of the report was adopted.

2. Report of the Committee on Legislation. This report was reviewed. On motions from the floor, a recommendation was amended to read that any physician in the state who knows a (state) legislator or his family notify the Association's Executive Secretary. This portion of the report was adopted, as amended.

3. Report of the Committee on Public Health. This report was reviewed and approved by the Reference Committee, with the recommendation that physical examinations be given at regular intervals as a requirement for continued drivers' licensure. Dr. Leigh asked that the House of Delegates go on record as favoring this idea. Speaker Christoferson suggested that the physical exam proposal could be referred to the Medical Advisory Committee to the State Highway Department, and be resubmitted at the Interim Meeting of the House in December, for specific recommendations to the Legislature. Dr. Dunnigan so moved. Seconded by Dr. Dahl and passed. This portion of the report was adopted, as amended.

4. The Reference Committee reviewed the subject of honorariums for speakers at state meetings, and proposed the establishment of a standard honorarium of $200.00 for out-of-state speakers at Annual Meetings. This portion of the report was adopted after amendment to leave the amount open, and to let the Council decide the amount a guest speaker should receive.

5. The Reference Committee noted the reports of the Committees on Public Relations and Official Publication, while pointing out neither had met during the year.

Dr. Little moved that the report be adopted as a whole, as amended. The motion was seconded by Dr. Leigh and carried.

Dr. James M. Little, *Chairman*
Dr. M. A. K. Lommen, *Vice-Chairman*
Dr. M. H. Poindexter, Jr.
Dr. Richard H. Leigh
Dr. Clayton E. Jensen

The meeting was reconvened after a recess of fifteen minutes.

Reference Committee to Consider the Report of the Committee on Medical Economics

The Reference Committee met with Executive Secretary Lyle Limond, in attendance, at which time Mr. Limond reported to it concerning correspondence with the Office for Dependents Medical Care which provided for a voluntary increase in fees for certain procedures: Tonsillectomy, Adenoidectomy, Dilation and Curettage. Inasmuch as the level of these fees was considered to be usual, customary, and reasonable, it was recommended by the committee that the proposed changes in the contract by ODMC be accepted, and that the contract be renewed.

Another item of business considered was referable to a letter written by W. B. Huntley, M.D., Minot, to the Indian Health Area Director in Aberdeen, S.D., in which Dr. Huntley refused to sign any contract with the Indian Bureau that did not consider usual and customary fees. It was felt that he expressed not only the philosophy of the Committee, but also that of the medical profession as a whole, and Dr. Huntley was commended for his action.

Next considered was the report of the Medical Economics Committee, which had been active since November, 1965. The Reference Committee was pleased to note that three meetings had been held, much work had been done, and the Committee commended those who had devoted their time and energy to it.

The Committee did feel, however, that some inconsistency was exhibited by the Medical Economics Committee in its December, 1965 meeting and objected to paragraph 1, on page 66 in the Handbook, which referred to negotiations with the Public Welfare Board. It was the feeling of the Committee that the concept of usual, customary, and reasonable fees be maintained with all public agencies, and that no negotiations should be necessary.

The Reference Committee asked that its report be adopted, with the exclusion of any reference to fees other than usual, customary and reasonable. This report was adopted.

(As a mater of information, Dr. Burt noted the following rulings of HEW, important from the standpoint of medical economics):

1. That no Carrier will be permitted to pay less to their subscribers than they pay for Medicare patients; and,

2. In a ruling as recently as last week, HEW has authorized any State Welfare Department to become a carrier, if they choose to do so.

Dr. A. C. Burt, *Chairman*
Dr. James J. Moses, *Vice-Chairman*
Dr. George H. Hilts
Dr. Kenneth S. Helenbolt
Dr. Donald E. Skjei
Dr. Richard S. Larson

Report of the Reference Committee on Resolutions to Include New Business

Dr. Vinje, chairman of the committee, submitted the following resolutions:

RESOLUTION No. 1

WHEREAS, the members of the North Dakota State Medical Association, attending the Seventy-ninth Annual Meeting of this Association in Fargo, have enjoyed the hospitality and consideration of this great city; and,

WHEREAS, the Mayor of Fargo and his associates, the Press, Radio, Hotels and businessmen have contributed to make this session a memorable one;

NOW, THEREFORE, BE IT RESOLVED that the House of Delegates express its appreciation by directing a copy of this Resolution to the Honorable Mayor of Fargo, and the Press.

This resolution was adopted.

RESOLUTION No. 2

WHEREAS, the members of the North Dakota State Medical Association, attending the Seventy-ninth Annual Meeting have thoroughly enjoyed and profited by an excellent scientific program; and,

WHEREAS, the Host, the First District Medical Society, and the various chairmen and committeemen have excelled in providing the members of the Association with the graciousness of a fine convention;

NOW, THEREFORE, BE IT RESOLVED that the assembled delegates demonstrate their appreciation by a rising vote of thanks.

A rising vote of thanks adopted this Resolution.

RESOLUTION No. 3

WHEREAS, the members of the North Dakota State Medical Association anticipate the increase in scientific knowledge to be gained from attendance at various exhibits; and,

WHEREAS, the Exhibitors have shown unusual effort, and ingenuity, in developing their exhibits and thereby adding to the scientific interest at this meeting;

NOW, THEREFORE, BE IT RESOLVED that the North Dakota State Medical Association extend to these Exhibitors our hearty welcome and thanks; and,

BE IT FURTHER RESOLVED that a copy of this Resolution be forwarded to each Exhibitor.

This resolution was adopted.

RESOLUTION No. 4

WHEREAS, Dr. J. D. Craven, President of the North Dakota State Medical Association for the year 1965-1966, did, in the years prior to his term of office, and in the year 1964-1965 as President-Elect of this Association, show an intense interest and devotion to the affairs and interests of the Association; and,

WHEREAS, with the aid of his experience, knowledge and concern relative to the practice of medicine in North Dakota, and with his dedication to the fulfillment of his office, Dr. Craven did, in such an exemplary manner, lead this Association through the past year;

NOW, THEREFORE, BE IT RESOLVED that the assembled delegates show their appreciation by a rising vote of thanks.

A rising vote of thanks adopted this Resolution.

RESOLUTION No. 5

WHEREAS, Mr. Lyle Limond and his competent staff have served the State Medical Association with diligence and proficiency during the immediate past year, as they have in preceeding years;

NOW, THEREFORE, BE IT RESOLVED that this House of Delegates formally show its appreciation with the adoption of this Resolution.

This resolution was adopted.

RESOLUTION No. 6

WHEREAS, the ladies of the Woman's Auxiliary to the North Dakota State Medical Association, through devoted enthusiasm, and continuous efforts over the years, have contributed diligently to the Medical Auxiliary Student Loan Fund of the Medical School of the University of North Dakota, and, more recently, to the American Medical Association Education and Research Foundation; and,

WHEREAS, these funds have enabled many medical students to complete their medical education; and,

WHEREAS, the local Auxiliary Societies throughout the State have participated in many other commendable projects which reflect credit to their organization and to the medical profession;

NOW, THEREFORE, BE IT RESOLVED that the House of Delegates of the North Dakota State Medical Association convey to the Woman's Auxiliary our appreciation and thanks for their excellent work; and,

BE IT FURTHER RESOLVED that a copy of this Resolution be directed to Mrs. M. A. K. Lommen, and her successor.

This resolution was adopted.

RESOLUTION No. 7

WHEREAS, an exhaustive and comprehensive study of the educational facilities training Doctors of Osteopathy in the United States has been made by Drs. Cleary and Nuessle; and,

WHEREAS, their conclusions are that:

(1) The 5 existing Osteopathic Schools in the U.S. have standards that do not meet the minimum requirements for medical schools;

(2) That the establishment of a composite examining board would be giving approval by the North Dakota State Medical Association of Osteopathic Schools as equal in training and standards to Medical Schools, when in fact they are not;

(3) That to approve a composite board of examiners, consisting of physicians, and D.O.'s would be prejudicial to the interests of the people of North Dakota and to the North Dakota State Medical Association;

NOW, THEREFORE, BE IT RESOLVED that the North Dakota State Medical Association concur in keeping the composition of the North Dakota State Board of Medical Examiners as presently prescribed by law; and,

BE IT FURTHER RESOLVED that the North Dakota State Medical Association oppose the formation of a composite board of medical examiners with doctors of osteopathy, and oppose the granting of full privileges of medical practice to Doctors of Osteopathy in North Dakota.

This resolution was adopted. (Excerpts from the discussion on the resolution follow).

SPEAKER: I believe it would be desirable at this time to read the Resolution that was passed at the last meeting of the House.

Resolution, passed in 1965

"WHEREAS, the Legislature is considering in future years giving osteopaths full practice privileges in the state of North Dakota; and,

WHEREAS, the medical profession recognizes that osteopathic schools have improved the standards of training and instruction in the scientific field in the past decade, and encourages further such improvement; and,

WHEREAS, this Association feels that doctors of medicine in the best interest of the people of the state of North Dakota in obtaining medical care of the highest quality, should be instrumental in overseeing the medical care in this state;

NOW, THEREFORE, BE IT RESOLVED that the House of Delegates favor consideration in the future of a composite Board of Medical Examiners made up of members of medicine and osteopathy, proportionate to now existing M.D.-D.O. population, providing adequate study by the interested parties has been carried out, referred back to the House at its next meeting, and final approval of the House of Delegates delayed until the proposed written bill can be reviewed."

This is being referred back to the House at this time, with the Resolution that the North Dakota State Medical Association oppose the Composite Board. This has been an exhaustive study by these two doctors.

DR. POWERS: These doctors, Cleary and Nuessle, have come to the conclusion that the establishment of a composite examining board would be giving approval of Osteopathic Schools, and this would be prejudicial to the interests of the people of North Dakota and the North Dakota State Medical Association, as these schools have not the training and standards of medical schools.

DR. LARSON: I would like to take a stand which would leave the door open for some future time.

SPEAKER: Dr. Mahoney is at this meeting and he is a legislator.

DR. MAHONEY: What is presented, and how it is worded, make quite a bit of difference in the legislature, and the way we wind up with a friendly position with the Osteopaths at this time. Two years ago there were approximately five or six Osteopaths in North Dakota over the age of 55 years. Those that talked to me did not want hospital privileges, but they would like it if there could be some form of an acceptance of young well trained men.

If the door can be left open; not to lower the practice of medicine, or lower the licensure, but to say in effect, "if you boys can pass our examinations, or you can practice the type of medicine practiced in North Dakota"—then you look for them to get their standards up—instead of saying a blunt "no."

At the present time, the legislators, many of them, if they come back, actually anticipate an affirmative recommendation for the Osteopaths from the Medics. With both the Osteopaths and the Medics, it was a very peaceful arrangement. We agreed there would be some thought put to it and we would try to come up with a positive recommendation on how this could be worked out in the future. We looked at some of the other states that were wrestling with this same problem, and we thought we could come up with some solution.

DR. MOSES: In the past their mood (Osteopaths) was such that they wanted us to allow them to practice the same type of medicine that we are practicing. We actually compromised to prevent the passage of that section. I believe if we go back with this resolution, the Osteopaths will have increased jurisdiction.

SPEAKER: If we pass this resolution, will a separate board be set up?

DR. MOSES: They have a separate board now, but they will be given more jurisdiction.

DR. DAHL: The most compelling reason for the Composite Board is the one that a composite board would give the State Board of Medical Examiners some control over the Osteopaths, and we would have more concentrated medical doctors on the Board. I think we have to take off from that point made by Dr. Moses. I do not think we will be able to provide a great deal of enforcement in Osteopathy with a Composite Board.

In Colorado they have a State Board of Examiners for Allied Arts, Osteopaths and Chiropractors, and Colorado has the largest Chiropractic Clinic in the United States, and they do not control that at all.

Drs. Cleary and Nuessle have found that the Osteopaths are not up to our standards, but if the legislature wants to force a composite board, then we can not help this. I think we should tell the people that these Osteopaths are not capable of practicing the type of medicine which we are capable of practicing.

DR. BEITHON: People are not going to remember that we did, or did not pass a resolution. I think if we fail to pass a resolution today, and give this more study and have William Daner, Attorney, work on this along with the Committee, and inquire from other states whether it works better with, or without a composite board, we could come up with a better resolution at the Interim Meeting.

SPEAKER: If this Resolution is defeated, then we would go back to the other Resolution passed last year in 1965 at the Annual Meeting.

DR. LITTLE: I think we have had an exhaustive study of this made. These doctors have come up with recommendations.

SPEAKER: Would you care to comment on this, Dr. Glaspel?

DR. GLASPEL: I read the report of the investigating committee. I did not disagree with it. I have not been well impressed in the past with these composite boards. Many states have them, and the Osteopaths feel that they are unwelcome guests. I would not be in favor of a composite board at all.

RESOLUTION No. 8

WHEREAS, the existing code regarding termination of pregnancy is unduly restrictive, as follows:

12-25-01. Procuring an abortion—Punishment.—Every person who administers to any pregnant woman, or who prescribes for any such woman, or who advises or procures any such woman to take, any medicine, drug, or substance, or uses or employs, or procures or advises the use, of any instrument or other means whatever, with intent thereby to procure the miscarriage of such woman, unless the same is necessary to preserve her life, shall be punished by imprisonment in the penitentiary for not less than one year, nor more than three years, or in a county jail for not more than one year.

WHEREAS, certain instances of pregnancy should be terminated which do not threaten the life of the mother such as pregnancy resulting from rape or incest,

NOW, THEREFORE, BE IT RESOLVED that the North Dakota State Medical Association recommends that Section 12-25-01 be amended to read:

"A licensed physician is justified in terminating a pregnancy if:

(a) He believes that if there is substantial risk that continuance of the pregnancy would gravely impair the physical or mental health of the mother or that the child would be born with grave physical or mental defect, or the pregnancy resulted from rape—or from incest; and,

(b) Three physicians, one of whom may be the person performing the abortion, have certified in writing their belief in the justifying circumstances, and have filed such certificates prior to the abortion in the licensed hospital where it is to be performed, or in such other place as may be designated by law."

BE IT FURTHER RESOLVED that since your Resolutions Committee is of the opinion that the North Dakota Law regarding abortion is in need of change, recommends to the House of Delegates that the above resolution be referred by the Speaker back to the Committee on Maternal and Child Welfare of the State Association, for investigation and specific language in finalized form for definitive legislative action, and presented to this House of Delegates for final action in December, 1966.

This resolution was adopted by adding an amendment that the Association President and State OB-GYN Society be notified of the meeting when the Maternal and Child Welfare Committee considers the resolution.

RESOLUTION No. 9

WHEREAS, there are hospitals in the State which do not have an adequate staff to organize a satisfactory Utilization and Review Committee; and,

WHEREAS, the new Medicare Law requires that there be such a Committee in each hospital for them to qualify;

NOW, THEREFORE, BE IT RESOLVED that the local medical society in each case offer their services in the formation of such a Committee, by furnishing the necessary numbers of outside men to sit with the active staff on these Committees.

This resolution was adopted with an amendment that physicians serving on Utilization Committees be compensated for time and travel.

DR. VINJE: The following resolution was submitted by the Northwest District Medical Society for consideration and action by the House of Delegates. This was referred by the Speaker to Reference Committee, number two, Dr. Countryman, Chairman. This reference committee approved of this resolution and referred it to our Committee for action.

RESOLUTION No. 10

WHEREAS, Section 2, Chapter IV (By-Laws) has created a problem of uncertainty as to the number of delegates to be seated at the time of local society elections;

BE IT THEREFORE RESOLVED THAT an addendum to Section 2, Chapter IV, read as follows:

"The number of delegates to be seated in the House of Delegates will be determined by the number of paid-up members as of December 31st, of the previous year;"

BE IT FURTHER RESOLVED that this proposed revision of the By-Laws be referred to the Committee on Constitution and By-Laws for its study and recommendation; and,

BE IT FURTHER RESOLVED that the House of Delegates make a decision of action at this Session of 1966, to be incorporated on second reading in 1966, according to the Constitution and By-Laws.

By a vote of 4 to 3, your Resolutions Committee rejected this Resolution.

I move that this Resolution be *not* accepted.

DR. GILTNER: I second the motion.

SPEAKER: I should like to read certain parts of the By-Laws on Page 17, of the Constitution and By-Laws:

Chapter IV, Section 2: Each component society shall be entitled to send to the House of Delegates each year, 1 delegate for each 15 members and 1 for each major fraction thereof, but each district society holding a charter from this association, which has made its annual report and paid its assessments as provided in this Constitution and By-Laws, shall be entitled to 1 delegate. In case a regularly elected delegate or alternate is unable to attend the annual meeting of the association, the speaker of the House of Delegates may appoint a substitute from the local society who shall have the rights and privileges of the regular delegates. Alternates may be seated in the House of Delegates but shall not be entitled to vote if the delegate for whom they are an alternate is present.

Page 28—Chapter IX, Section 2: Any district society which fails to pay its assessment, or make the report required, on or before the first day of April in each year, shall be held as suspended, and none of its members of Delegates shall be permitted to participate in any of the business or proceedings of the Society or of the House of Delegates until such requirements have been met.

SPEAKER: This is now open for discussion.

DR. POWERS: I appeared before Dr. Countryman's committee, but I did not appear before the Resolutions Committee. If you stick to the way the Constitution and By-Laws read, right now delegates of the First, Third and Fourth and Sixth Districts would not be seated. If the total assessments were not paid by April 1st, none of your delegates would be seated. It would be a thin meeting. Right now, if someone rose to a point of order, we would not any of us be here.

I refer you to page 14 in your Handbook, under the Secretary's Report. Table I shows the annual members for the past five years; Table II shows the annual dues payments according to the cut-off date for preparation of the report, for the past five years. This constitutes a difference of from 47 to 64 members who paid their dues after the deadline. Apparently fifty people in the Society are being denied representation, because they are paying $100.00 for the year and are getting no representation, if they do not pay their dues by the time of the state meeting. And, if this is the case, why should they bother to pay them—they might as well use them for their next year's dues if you are not going to give them the representation. We have people in our society that we never see. They do not come to our meetings. They could care less if we have no delegates, but every year they pay their $100.00. I believe they are still entitled to representation. Most of the Societies hold their elections in January or February. We are guessing as to how many delegates we are to elect. We get no letter from the State Association as to how many delegates we are entitled to. I think the only logical thing to do, is this. You know how many are paid up the previous year. You can use that figure for your election. I never know, even though I am elected to be a delegate, whether I am going to be seated as a delegate at the State Meeting until the day before the meeting.

The Council should not have to call the secretaries of the district societies the night before the meeting and tell them they are short one paid-up member to seat their elected number of delegates. It does not matter what date you set for them to pay their dues, there are some that are going to be late. They have been doing this for 25 years and it is not going to change them. Most of us pay our dues, or at least the same guys pay the same month over the years. They say they need the money for operating expenses, but we have in reserve $45,000.00 —one full year's operating budget. I feel that for the first three months of any year, we are not going to go broke.

The way the By-Laws are written now are not right. I think this should be changed. I think this present Resolution would do this. It has been done once and it could be acted upon at this session.

DR. BRIGGS: I would like to give a minority report. We discussed this in our Committee meeting. A few things have occurred to me in listening to the By-Laws. There are a lot of members in the various district societies that will pay their dues sometime during the year. Yet, the Secretary would be unwilling to pay the society's assessment by the first of April so that they could all be seated, as he is not quite sure they will all pay by the end of the year. Why not have the local society pay up their assessment by the first of April, such as they need, to get all the delegates seated, and then the local society is under pressure to get these dues in before the first of the year. Then we would have the dues in by the first of April and this would put the problem of collecting back on the shoulders of the district society.

DR. HELENBOLT: I am rather proud of Dr. Powers' eloquent presentation. However, it seems to me that there might be some members of a certain group that would move elsewhere to practice, or become deceased, and this should be taken into consideration when paying dues of the members.

DR. LITTLE: I think this is a way to get our dues in. If there is no hurry for us to send in our dues, then it would be ridiculous to pay our dues in January. We could put our money in C.D.'s and collect the interest and wait to pay our dues for six months, making some interest on this money for ourselves.

If you do not pay your dues for one year, you are not a member of the State Medical Association. If you are not a member of the State Medical Association, you are not a member of Blue Shield. I feel we should pay our dues when they are assessed, and those who are chronically late, should be penalized by not being represented.

DR. POWERS: The fact came out that you could not belong to any Malpractice, if you were not a member. However, you do not have to be a member of the State Medical Association to be eligible for Malpractice. Also, in regard to being a participating member of Blue Shield, Mr. Eagles brought in an opinion, and Mr. Vogel gave an opinion, under the Enabling Act that anyone licensed to practice medicine is eligible to be a member of Blue Shield. It is in the By-Laws that you should be a member of the Association but it could not be adhered to legally.

DR. BRIGGS: It occurred to me regarding the people who should be represented here at the meetings, if some of these fellows have not been seen at these meetings for five or ten years, I do not know how the delegates could represent these people, if they have not talked to them.

DR. LEIGH: One of the major drives behind this change in the By-Laws is that it should make no difference whether the dues are paid in the current year, or the year following. I would like to see that change go through.

SPEAKER: We have a motion that this Resolution be *not* adopted.

DR. POWERS: The committee that referred this to the Resolutions Committee recommended that this be adopted. The Resolutions Committee turned this down. In order to support the change in the By-Laws, you would have to vote No.

SPEAKER: All those in favor of the Resolution *not* being adopted? A "yes" vote will mean that this is not adopted. If you vote this down, you will have to have a new resolution.

SPEAKER: You are simply turning down the Resolution if you vote "yes" to the motion. All those in favor of this *not* being adopted? None. —Motion is not accepted.

DR. POWERS: I move that the original motion as submitted by Reference Committee number two; which is the same as the resolution submitted to the House last year; be accepted.

DR. COUNTRYMAN: I second the motion.

SPEAKER: I will read the Resolution submitted to the House of Delegates in 1965:

WHEREAS, Section II, Chapter IV (By-Laws) has created a problem of uncertainty as to the number of delegates to be seated at the time of local society elections;

BE IT THEREFORE RESOLVED, an addendum to Section II, Chapter IV, read as follows:

"The number of delegates to be seated in the House of Delegates will be determined by the number of paid-up members as of December 31st, of the previous year."

BE IT FURTHER RESOLVED that this proposed revision of the By-Laws be referred to the Committee on Constitution and By-Laws for its study and recommendation; and,

BE IT FURTHER RESOLVED the House of Delegates make a decision of action at this session of 1965, to be incorporated on second reading in 1966, according to the Constitution and By-Laws.

Chapter XIV, "Amendments" of the Constitution and By-Laws, is as follows:

"These By-Laws may be amended at any annual session by a two-thirds vote of all delegates present at that session. Any such amendment may be introduced at any session of the House of Delegates but shall be laid upon the table for that current session and acted upon at any later session of the House of Delegates."

Ayes, 26; Opposed, 4. The Resolution is adopted and the By-Laws are hereby amended.

RESOLUTION No. 11

WHEREAS, hospital based medical specialists (physiatrists, radiologists, pathologists, and anesthesiologists) are engaged in the practice of medicine; and,

WHEREAS, the services of such specialists should not be merged with hospital charges;

NOW, THEREFORE, BE IT RESOLVED that the House of Delegates of the North Dakota State Medical Association subscribe to the principle that the charges of such specialists should be established, billed and collected by the Medical Specialists in the same manner as are the fees of other physicians.

This resolution was adopted.

RESOLUTION No. 12

WHEREAS, any arrangement between government and a citizen whereby the government agrees to pay for the citizen's medical care does not, directly or indirectly, or by inference, involve the physician in a contract with the government; and,

WHEREAS, once a physician accepts a person as his patient, his primary and sole obligation, his contract and his relationship are with the patient, regardless of what third party may be involved;

NOW, THEREFORE, BE IT RESOLVED that the House of Delegates of the North Dakota State Medical Association suggest and urge the members of this Association to deal directly with the patient, both in providing medical care and in billing for just and reasonable compensation for the medical care provided; and,

BE IT FURTHER RESOLVED that in accordance with the Principles of Medical Ethics, that each and every member of this Association submit to the patient his own bill and receive on his own behalf, compensation for his professional medical services.

DR. BRIGGS: When you mention in this resolution "third party" you are talking about our dealings with the patient who has as a third party the Federal Government, or do you mean any third party? Would this include our dealings with the North Dakota Physicians Service? Are we taking two dissimilar positions in regard to third parties?

DR. VINJE: This includes this, but it does not preclude the Physicians Service paying you directly.

This resolution was adopted by striking the words "and only" from line 3, paragraph 3, to make the resolution read as printed above.

Dr. Vinje moved that the report as a whole, as amended, be adopted. The motion was seconded by Dr. Dahl and carried.

Dr. Edmund G. Vinje, *Chairman*
Dr. Edwin O. Hieb, *Vice-Chairman*
Dr. Lloyd A. Giltner
Dr. John A. Sandmeyer
Dr. Paul J. Beithon
Dr. Walter C. Hanewald
Dr. Phillip O. Dahl

SPEAKER: I would now like to call on a report from the Treasurer, with his recommendation as to the dues for the State and National.

DR. NIERLING: One of these last items brought up rather interested me, being Treasurer, as to how and when the dues could be paid this year. It really does not make much difference. The main purpose of the Treasurer is to see that these dues get in. I would still recommend that you get these in after the first of January, and keep trying until you do get them in. It does help to keep our books up to date at the time of the Annual Meeting.

On page 18 of the Handbook is the Treasurer's report. I will not go into detail on this report. We expect this year approximately the same amount from dues. We have tried an innovation this year which has never been done before. It was suggested by the Council at the December meeting, if the dues come in early and a good many of them do, we have in the account approximately some $40,000.00 which we do not need at the present time. It was suggested by the Council that some of this money be taken out and placed on C.D.'s on a term of three or six months, depending upon how soon we would need the money for the operation of the office. We did this and at the present time, we have $10,000.00 on six months C.D.; $5,000.00 on three months C.D.; and $11,000.00 in the general fund which we have not taken out for that purpose. The main expenditures of the Association come from the Executive Secretary's office. Mr. Limond calls for this money to operate his office and his salary, and he calls for this by thirds, so we can actually keep these C.D.'s and add some interest. At the end of the year it will be interesting to see the results.

Incidentally, while I am here, I would like to talk for just a moment on the basis of a local society treasurer, because I have been a treasurer of the local society. Many years ago, the Secretary had no dues to collect except $5.00 for his local group. Now we have reached a point, in the Seventh District, that we have collected the Local, State, AMA, and Woman's Auxiliary; and for many meals in advance for the local society meetings. About a year or so ago we decided to collect for the meals for the doctors ahead of time to see if we could make them come to the meetings. As a result, we have collected from the doctors in the Seventh District about $200.00 per year, $20.00 of which is for the Woman's Auxiliary. This is the first time this has been done. This was at the recommendation of the Council and no one objected to it. All the husbands paid it. I think all groups should do this.

As far as the budget is concerned, for the coming year, it was a little higher but we still feel we can operate within that amount. That is the budget proposed at the beginning of the year and is not the actual amount spent each year. Sometimes we have a little left over; sometimes we have saved the money from the proposed budget over the course of a year. We have operated in the black. We do not feel, providing we can continue to operate in the black, that there is a necessity to increase the dues over $100.00.

I move that the state dues be $100.00 per person for the year 1967.

DR. VINJE: I second the motion.

SPEAKER: Is there any discussion? All in favor? All Ayes. Motion passed, and the dues are $100.00 for 1967.

DR. NIERLING: I believe we discussed the National dues at one of the committee meetings, and a recommendation was passed. Therefore, Dr. Pederson knows what he should do.

SPEAKER: In last year's minutes we voted to have our meeting in Jamestown in 1967, and in Bismarck in 1968. For the purpose of the minutes, I would like to have Dr. Miles move that the meeting be held somewhere else than in Jamestown in 1967.

DR. HEIB: I would like to retract that invitation as our facilities in Jamestown have not materialized.

An invitation was extended by Dr. Dahl to the members of the Association to hold their 1967 meeting in Bismarck. This motion passed.

Dr. Beithon moved that the Interim Meeting be held December 10, 1966 in Fargo, as recommended by the Council. The motion was seconded by Dr. Sandmeyer and carried. Dr. Dunnigan then moved that this motion be rescinded and the meeting date be changed to December 11, 1966 at Fargo, N.D. This motion was seconded by Dr. Countryman and passed. There was no motion for a meeting place in 1968.

The following is the report of the Nominating Committee. During the presentation of the slate of nominees, Dr. Christoferson announced his wish to resign as Speaker of the House. He added that he appreciated the honor given him, but felt that the Speaker of the House of Delegates should be kept but a few number of years, and then rotated through the Association. He further stated that the position is a very important one, and therefore, he felt there was a need for the Association to change speakers at periodic intervals.

In view of the fact that Dr. Dahl was serving a 2 year term as Vice-Speaker, Dr. Dodds, Chairman of the Nominating Committee, asked the House to select a Vice-Speaker for the year as he had no authority to act in that regard. Dr. Leigh nominated Dr. Countryman for Vice-Speaker of the House of Delegates. A unanimous ballot was cast for Dr. Countryman.

The slate of nominees, as presented by the Nominating Committee, was voted on singly as follows:

President	G. W. TOOMEY, Devils Lake
President-Elect	V. J. FISCHER, Minot
First Vice-President	C. H. PETERS, Bismarck
Second Vice-President	R. C. PAINTER, Grand Forks
Secretary	W. M. BUCKINGHAM, Bismarck
Treasurer	R. D. NIERLING, Jamestown
Delegate to the AMA	T. PEDERSON, Jamestown
Alternate Delegate to the AMA	JAMES MOSES, Bismarck
Speaker of the House of Delegates	P. DAHL, Bismarck
Vice-Speaker of the House	G. L. COUNTRYMAN, Grafton

Nominated as councillors were Drs. R. W. McLean, Tenth District and C. J. Klein, Fifth District. Nominated from the Fourth District were Drs. R. S. Larson, Brian Briggs and G. Richardson. Dr. R. S. Larson was elected councillor for the 4th District.

Board of Medical Examiners

The names of three physicians, present members of the Board of Medical Examiners whose terms expire in 1966, were to be submitted to the Governor for appointment to the Board: C. M. Lund, Williston; G. Wilson Hunter, Fargo; F. R. Erenfeld, Minot. Dr. Powers moved that the nominations cease, and that the names of these three men be submitted to the Governor for appointment to the Board of Medical Examiners. The motion was seconded by Dr. Amidon and passed.

At this time Dr. Briggs made a motion that copies of the 1966 proceedings be provided for the delegates at the 1967 meeting of the Association, either in the form of mimeographed sheets or Journal Lancet sheets. This motion was seconded by Dr. Larson and passed.

SPEAKER: I would like at this time to personally thank Lyle Limond and his staff for the wonderful job they have done for this meeting. As retiring Speaker of the House, I would like to discuss with you what I would like to have happen in the future.

In the last ten or fifteen years, we have seen a resurgence of interest in the Association's actions, with up and coming delegates at the annual meetings. Unfortunately, I feel this has not happened with the AMA. What we pass on a state basis is only what has already been passed upon in the AMA. I recognize that there are some 69 measures coming before the House of Delegates of the AMA. I feel strongly that this body should instruct our AMA Delegates what they wish to have done. Unless what is happening here continues on to the upper echelons, I am afraid we will see our actions lost.

I, therefore, would urge and plead, in spite of the fact that it would take a lot of time and increase the duration of the meeting of this House, that our Delegate to the AMA try to include in his report, those matters of business that are going to come up before the AMA meeting, as a part of business to be discussed in this Association; so that action can be taken here before National action is taken on it. I think in this way we are going to have a better over-all approach.

It has been really a rewarding experience to be Speaker of this House. I am sure Dr. Dahl will benefit by his association with you.

Adjournment was at 5:00 P.M.

SCIENTIFIC PROGRAM

Friday, April 29, 1966

CIVIC MEMORIAL AUDITORIUM – FARGO, N.D.

9:00 A.M. – Registration

10:30 A.M. – Welcome
Blaine Amidon, M.D., President, First District Medical Society
Mayor of Fargo.

10:30 - 11:15 A.M. – "Organ Replacement," Richard C. Lillehei, M.D., Associate Professor of Surgery, University of Minnesota. (Sponsored by the North Dakota Heart Association.)

11:15 - 12:00 Noon – "Genetics and Behavior in Mental Retardation," V. Elving Anderson, Ph.D., Associate Professor of Genetics, University of Minnesota.

NOON RECESS – EXHIBIT VISITATION

2:00 - 2:30 P.M. – "Management of Carcinoma of the Rectum," Dale B. Flickinger, M.D., Medical Arts Clinic, Minot, North Dakota. (Sponsored by the American Cancer Society, North Dakota Division, Inc.)

2:30 - 3:00 P.M. – "The Incidence of Heart Disease in Incoming Freshmen at the University of North Dakota–An Eight-Year Study," Edwin G. Olmstead, M.D., Associate Professor of Medicine, University of North Dakota. (Sponsored by the North Dakota Heart Association.)

3:00 - 3:30 P.M. – INTERMISSION – EXHIBIT VISITATION

3:30 - 4:15 P.M. – "Shock," Richard C. Lillehei, M.D., Associate Professor of Surgery, University of Minnesota. (Sponsored by the North Dakota Heart Association.)

4:15 - 5:00 P.M. – "Complications in Antimicrobial Therapy," William J. Martin, M.D., Associate Professor of Medicine, Mayo Foundation Graduate School, University of Minnesota.

Saturday, April 30, 1966

CIVIC MEMORIAL AUDITORIUM – FARGO, N.D.

9:00 A.M. - 3:30 P.M. – Registration

10:30 - 12:00 Noon – "Recent Advances in the Management of Rh. Isoimmunization."

(a) "Amniocentesis and Early Delivery," John M. Bowman, M.D., Assistant Professor of Pediatrics, Clinical Director of the Rh. Laboratory, University of Manitoba.

(b) "Intraperitoneal Transfusion," Rhinehart F. Friesen, M.D., Lecturer and Senior Research Assistant, Department of Obstetrics and Gynecology, University of Manitoba.

NOON RECESS – EXHIBIT VISITATION

Compact Luncheon, Hoyt Gardner, M.D., Guest Speaker

2:00 - 2:30 P.M. – "The Epidemic of Coronary Artery Disease," Gunther H. Heidorn, M.D., Minot, N.D. (Sponsored by the North Dakota Heart Association.)

2:30 - 3:00 P.M. – "The Chemotherapy of Solid Tumors," Robert O. Johnson, M.D., Assistant Professor, Division of Clinical Oncology and Department of Surgery, University of Wisconsin Medical Center. (Sponsored by the American Cancer Society, North Dakota Division, Inc.)

3:00 - 3:30 P.M. – Intermission

3:30 - 4:30 P.M. – "Undersea Living–Project Sealab II," Captain George F. Bond, M.D., U.S.N., Special Projects Office, Department of the Navy, Washington, D.C.

North Dakota State Medical Association Roster—1966

MEMBERSHIPS BY DISTRICTS

First District

Amidon, Blaine F.	Dakota Clinic, Fargo
Armstrong, Wm. B.	801 6th Ave. No., Fargo
Bacheller, Stephen C.	Enderlin
Bakke, Hans	Lisbon
Barnard, Donald M.	Fargo Clinic, Fargo
Bart, Bruce J.	Fargo Clinic, Fargo
Beithon, Elmer J.	Red River Valley Clinic, Wahpeton
Beithon, Paul J.	Red River Valley Clinic, Wahpeton
Beltz, Melvin E.	Wahpeton Clinic, Wahpeton
Bjerke, Leon A.	Red River Valley Clinic, Wahpeton
Borland, Verl G.	Fargo Clinic, Fargo
Burt, Arthur C.	Medical Arts Bldg., Fargo
Bushell, Robert P.	Fargo Clinic, Fargo
Christoferson, Lee A.	700 1st Ave. South, Fargo
Christu, Chris M.	Fargo Clinic, Fargo
Darrow, Kent E.	Dakota Clinic, Fargo
DeCesare, Francis A.	Dakota Clinic, Fargo
Dillard, James R.	Veterans Administration, Fargo
Dodds, G. Alfred	Fargo Clinic, Fargo
Donat, T. L.	Medical Arts Bldg., Fargo
Ehlen, Matt J.	Fargo Clinic, Fargo
Engstrom, Perry H.	Red River Valley Clinic, Wahpeton
Fercho, Calvin K.	Medical Arts Bldg., Fargo
Fortney, Arthur C.	Fargo Clinic, Fargo
Foster, George C.	1602 South 6th Street, Fargo
Gaebe, Robert C.	700 1st Avenue South, Fargo
Geib, Marvin J.	700 1st Avenue South, Fargo
Geston, Robert L.	402 Sheyenne St., West Fargo
Gillam, John S.	Fargo Clinic, Fargo
Goff, John R.	Fargo Clinic, Fargo
Goltz, Neill F.	Fargo Clinic, Fargo
Gustafson, Maynard	700 1st Avenue South, Fargo
Hall, G. Howard	Fargo Clinic, Fargo
Halliday, D. Ross	Fargo Clinic, Fargo
Hamilton, Thomas M.	Fargo Clinic, Fargo
Hawn, Hugh W.	Gate City Building, Fargo
Haynes, George H.	Lisbon
Heilman, Charles O.	Fargo Clinic, Fargo
Houghton, James F.	Dakota Clinic, Fargo
Hunter, C. M.	Medical Arts Building, Fargo
Hunter, G. Wilson	Fargo Clinic, Fargo
Irvine, Vincent S.	Lidgerwood
Ivers, Robert R.	700 1st Avenue South, Fargo
Jaehning, David G.	Hotel Wahpeton, Wahpeton
Jordheim, Robert	Fargo Clinic, Fargo
Kana, Dale C.	Medical Arts Building, Fargo
Kelly, William A.	Medical Arts Building, Fargo
Kohlmeyer, A. C.	700 1st Avenue South, Fargo
Kulland, Roy E.	402 Sheyenne Street, West Fargo
Lamb, Donald L.	Medical Arts Building, Fargo
Lancaster, W. E. G.	Rt. 1, Detroit Lakes, Minnesota
Landa, Marshall	Dakota Clinic, Fargo
Lane, Mark H.	700 1st Avenue South, Fargo
Larson, G. Arthur	1538 9th Street South, Fargo
Lawrence, Donald H.	N.D. State U., Fargo
LeBien, Wayne E.	Fargo Clinic, Fargo
Leegard, Robert L.	Fargo Clinic, Fargo
LeMar, John D.	Fargo Clinic, Fargo
Levine, Leonard	Fargo Clinic, Fargo
Lewis, A. K.	Lisbon
Lewis, T. H.	302 Black Building, Fargo
Lindsay, Douglas T.	Fargo Clinic, Fargo
Lytle, Francis T.	Fargo Clinic, Fargo
McMahon, John M.	Dakota Clinic, Fargo
Macaulay, Warren L.	Fargo Clinic, Fargo
Magill, Gordon B.	Medical Arts Building, Fargo
Mazur, Bernard A.	Dakota Clinic, Fargo
Melton, Frank M.	Dakota Clinic, Fargo
Miller, Herbert H.	509½ Dakota Avenue, Wahpeton
Miller, Joseph W.	Dakota Clinic, Fargo
Murray, James B.	Dakota Clinic, Fargo
Nagle, Duane W.	Fargo Clinic, Fargo
Nord, J. Erling	Medical Arts Building, Fargo
Norum, Henry A.	Fargo Clinic, Fargo
Obert, Gerard J.	St. Luke's Hospital, Fargo
Ohrt, Harry A.	Medical Arts Building, Fargo
O'Hearn, Jerome W.	Fargo Clinic, Fargo
Olafson, Richard A.	700 1st Avenue South, Fargo
Olin, Ronald	Fargo Clinic, Fargo

Oliver, James	Medical Arts Building, Fargo
Palmer, Wesley J.	Lisbon
Poindexter, M. H.	Fargo Clinic, Fargo
Poole, Ernest E.	Lidgerwood
Pray, Laurence G.	Fargo Clinic, Fargo
Rogers, Robert G.	Dakota Clinic, Fargo
Schleinitz, Fritz B.	Hankinson
Schneider, Joseph F.	Medical Arts Building, Fargo
Schutt, Ann H.	700 1st Avenue South, Fargo
Sedlak, Oliver A.	109 Roberts Street, Fargo
Seifert, Richard H.	Medical Arts Building, Fargo
Shook, Lester D.	Fargo Clinic, Fargo
Spier, J. J.	Dakota Hospital, Fargo
Stafne, William A.	2701 12th Street South, Fargo
Story, Robert D.	Fargo Clinic, Fargo
Swanson, Joel C.	1220 8th Street South, Fargo
Thompson, George R.	Fargo Clinic, Fargo
Thorfinnson, Hugh D.	Medical Arts Building, Fargo
Traynor, Mack V.	Fargo Clinic, Fargo
Triggs, Perry O.	Fargo Clinic, Fargo
Ulmer, Robert J.	Dakota Clinic, Fargo
Veitch, Abner	Lisbon
Wall, Wendell H.	Wahpeton Clinic, Wahpeton
Wasemiller, E. R.	Wahpeton Clinic, Wahpeton
Webster, William O.	Fargo Clinic, Fargo
Weible, Earl B.	Abercrombie
Weible, Ralph D.	Dakota Clinic, Fargo
Wenz, E. P.	Dakota Clinic, Fargo
Wenzel, James B.	Dakota Clinic, Fargo
Weyers, Henry J.	402 Sheyenne Street, West Fargo
Williams, N. S.	Dakota Clinic, Fargo
Wiltse, Glenn L.	Wahpeton Clinic, Wahpeton
Wold, Lester E.	Fargo Clinic, Fargo

Second District

Cook, Stuart J.	Rolette
Corbett, Conner A.	Lake Region Clinic, Devils Lake
Coultrip, Raymond L., Jr.	McVille (In Service)
Engesather, J. A. D.	Lakota
Eylands, Jon V.	Johnson Clinic, Rugby
Fawcett, John C.	Lake Region Clinic, Devils Lake
Fawcett, Robert M.	Lake Region Clinic, Devils Lake
Fox, William R.	Johnson Clinic, Rugby
Gilbertson, Erest V.	Lake Region Clinic, Devils Lake
Glasner, Duane D.	Rolla
Hillman, R. S. Lyle	Johnson Clinic, Rugby
Hilts, George H.	Cando
Johnson, C. G.	Johnson Clinic, Rugby
Kihle, Kenneth W.	Bottineau
Klassen, Leonard	Rolette
Lazareck, I. L.	411 Fourth Avenue, Devils Lake
Lind, Jackson W.	Bottineau
Lund, A. B.	Leeds
McBane, R. Donald	Lake Region Clinic, Devils Lake
McIntyre, Donald G.	Johnson Clinic, Rugby
Mahoney, James H.	411 Fourth Avenue, Devils Lake
Mari, Justo L.	Bottineau
Martin, George V.	Michigan
Miller, C. Robert	Bottineau
Mimay, Antonio	Maddock
Neuenschwander, Allen R.	Rolla
Overland, Arnold J.	Rolla
Owens, Clarence G.	New Rockford
Pine, Louis F.	Lake Region Clinic, Devils Lake
Rinn, David A.	Cando
Sawchuk, John	Rolette
Schwinghamer, E. J.	New Rockford
Seibel, Glenn W.	New Rockford
Terlecki, Jaroslaw	Minnewaukan
Toomey, Glenn W.	Lake Region Clinic, Devils Lake
Towarnicky, Marvin J.	Fessenden
Turkula, William	Lake Region Clinic, Devils Lake
Voglewede, William C.	Carrington
Wolf, Jerry D.	Bottineau

Third District

Barcome, Donald F.	U.N.D., Grand Forks
Barrie, James G.	Park River
Benson, T. Q.	1600 University Avenue, Grand Forks
Benwell, Harry D.	California (retired)
Bowes, H. Angus	1600 University Avenue, Grand Forks
Clark, Rodney	Grand Forks Clinic, Grand Forks
Clayburgh, B. J.	201 South 4th Street, Grand Forks
Countryman, G. L.	1004 Hill Avenue, Grafton
Culmer, A. E., Jr.	501 1st Natl. Bank Bldg., Grand Forks
Dailey, Walter C.	Valley Medical Associates, Grand Forks
DeLano, Robert H.	Northwood
Doss, R. Douglas	1600 University Avenue, Grand Forks
Eaton, L. P.	Grafton Clinic, Grafton
Engelstad, Orlyn D.	U.N.D., Grand Forks
Evans, Harold W.	Grand Forks Clinic, Grand Forks
Flaten, Alfred N.	Edinburg
Glaspel, Cyril J.	Grafton Clinic, Grafton
Goehl, R. O.	Grand Forks Clinic, Grand Forks
Graham, Charles M.	1600 University Avenue, Grand Forks
Graham, John H.	31½ South Third, Grand Forks
Grinnell, Ernest L.	Grand Forks Clinic, Grand Forks
Hardy, Nigel A.	Minto
Harwood, T. H.	Medical School, U.N.D., Grand Forks
Haugen, C. O.	Larimore
Haunz, Edgar A.	Grand Forks Clinic, Grand Forks
Helenbolt, Kenneth S.	1600 University Avenue, Grand Forks
Helgason, Norman M.	Cavalier
Helm, Richard K.	Valley Medical Associates, Grand Forks
Hill, Frank A.	Grand Forks Clinic, Grand Forks
Isaacson, Peter G.	U.N.D., Grand Forks
Jensen, August F.	Mesa, Arizona (retired)
Johnson, Curtis A.	Valley Medical Associates, Grand Forks
Kaluzniak, Nicholas	Langdon
Keig, William P., Jr.	1600 University Avenue, Grand Forks
Krahn, Henry	Walhalla
Lambie, John A.	Grand Forks Clinic, Grand Forks
Landry, L. H.	Walhalla
Larson, Eric J.	Cavalier
Leigh, James A.	111 North 5th St., Grand Forks
Leigh, Ralph E.	111 North 5th St., Grand Forks
Leigh, Richard H.	1600 University Avenue, Grand Forks
Lorentson, Carl E.	Grand Forks Clinic, Grand Forks
McKay, John F.	703 South 4th Street, Grand Forks
McLaughlin, Blaine E.	U.N.D., Grand Forks
McLeod, John	201 South 4th Street, Grand Forks
Mahowald, Ralph E.	1400 Grand Ave., Grand Forks
Mann, Hamish	1600 University Avenue, Grand Forks
Marshall, Robert A.	27 S. Third St., Grand Forks
Meredith, William C.	Drayton
Muus, Jacob M.	McVille
Muus, O. Harold	27½ S. Third St., Grand Forks
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Nelson, William C.	Grand Forks Clinic, Grand Forks
Olson, James R.	Grand Forks Clinic, Grand Forks

Painter, Robert C.	Grand Forks Clinic, Grand Forks
Panek, Adam F.	Milton
Pansegrau, Duane F.	Grand Forks Clinic, Grand Forks
Peake, Frances M.	14½ S. Third St., Grand Forks
Penners, John H.	Grand Forks Clinic, Grand Forks
Pettit, Samuel L.	Grand Forks Clinic, Grand Forks
Piltingsrud, Harold R.	Park River
Pinsonneault, Wilfrid A.	Drayton
Powers, William T.	Valley Medical Associates, Grand Forks
Prochaska, Leonard J.	517 1st Natl. Bank Bldg., Grand Forks
Ralston, Lloyd S.	33½ S. Third Street, Grand Forks
Rand, Charles C.	State School, Grafton
Rice, Edwin G.	Grand Forks Clinic, Grand Forks
Ruud, John E.	1st Natl. Bank Bldg., Grand Forks
Saiki, A. K.	U.N.D., Grand Forks
Sande, C. W.	Northwood
Sandmeyer, John A.	Grand Forks Clinic, Grand Forks
Schafer, Thomas	Grand Forks Clinic, Grand Forks
Scheflo, Myron W.	1004 Hill Avenue, Grafton
Silverman, Louis B.	Grand Forks Clinic, Grand Forks
Tarpley, Harold I.	Valley Medical Associates, Grand Forks
Teevens, William P.	Grafton Clinic, Grafton
Thorgrimsen, G. G.	1600 University Avenue, Grand Forks
Tompkins, C. R.	1004 Hill Avenue, Grafton
Vandergon, Keith G.	1400 Grand Ave., Grand Forks
Wasdahl, Walter	U.N.D., Grand Forks
Webber, Freeman B.	Harvey
Wilson, George A.	Grand Forks Clinic, Grand Forks
Wilson, Russell H.	U.N.D., Grand Forks
Woutat, Philip H.	Grand Forks Clinic, Grand Forks
Youngs, Nelson A.	Grand Forks Clinic, Grand Forks

Fourth District

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Blatherwick, Robert	Parshall
Boyle, John T.	Garrison Clinic, Garrison
Boyum, Lowell E.	Harvey Medical Center, Harvey
Breslich, Paul J.	Northwest Clinic, Minot
Briggs, Brian E.	Main Medical Bldg., Minot
Cameron, Angus L.	Northwest Clinic, Minot
Cameron, A. Malcolm	Northwest Clinic, Minot
Devine, John L., Jr.	Great Plains Clinic, Minot
Dormont, Richard E.	Northwest Clinic, Minot
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Fischer, V. J.	Medical Arts Clinic, Minot
Flath, Milford G.	Stanley
Flickinger, Dale B.	Medical Arts Clinic, Minot
Gammell, Robert T.	Kenmare
Garrison, M. W.	Garrison Building, Minot
Giltner, Lloyd A.	Medical Arts Clinic, Minot
Goodman, Robert	Powers Lake
Halliday, David J.	Kenmare
Halverson, C. H.	401 South Main, Minot
Hammargren, August F.	Harvey Medical Center, Harvey
Hart, George M.	Northwest Clinic, Minot
Heidorn, G. H.	Main Medical Building, Minot
Hiliopoulos, D.	Westhope
Hoopes, L. L.	315 South Main, Minot
Hordinsky, B. Z.	Drake
Huntley, Wellington B.	315 South Main, Minot
Hurly, William C.	Medical Arts Clinic, Minot
Huss, Bernard	Medical Arts Clinic, Minot
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Kaljot, Victor	Northwest Clinic, Minot
Keck, Stanley W.	Northwest Clinic, Minot
Kermott, L. H., Jr.	401 Main Street South, Minot
Kohl, D. L.	123 2nd Avenue S.E., Minot
Lampert, M. T.	407 1st Natl. Bank Bldg., Minot
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Leonard, Kermit	Garrison Clinic, Garrison
London, Carl B.	Northwest Clinic, Minot
Naegeli, Frank D.	Northwest Clinic, Minot
Natarajan, Rangasamy	Main Medical Building, Minot
Nazli, Mehmet	401 South Main, Minot
Odegard, Russell L.	Great Plains Clinic, Minot
Olson, Burton G.	McCannel Clinic, Minot
Richardson, Gale R.	Main Medical Building, Minot
Ringo, G. Roy	119-A South Main St., Minot
Rioux, Berchmans	14-A South Main, Minot
Rowe, Paul H.	Northwest Clinic, Minot
Sahl, Jens, Jr.	Northwest Clinic, Minot
Shea, Samuel E.	McCannel Clinic, Minot
Sorenson, Alfred R.	Medical Arts Clinic, Minot
Sorenson, Roger	Medical Arts Clinic, Minot
Uthus, O. S.	21½ 2nd Avenue S.E., Minot
Vandersteen, Paul R.	Medical Arts Clinic, Minot
Veenbaas, Fred F.	Northwest Clinic, Minot
Wall, Willard W.	Northwest Clinic, Minot
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Westervelt, A. E.	Bowdon
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Fifth District

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Craychee, Walter A.	Oakes
Feist, Donald J.	Forman
Goven, John W.	Valley City Clinic, Valley City
Hockenberry, James A.	Oakes
Jensen, Clayton E.	Valley City Clinic, Valley City
Jensen, Warren R.	117 N.W. Third, Valley City
Klein, C. J.	Valley City Clinic, Valley City
Macdonald, Alexander C.	130 Central Avenue South, Valley City
Macdonald, Neil A.	130 Central Avenue South, Valley City

Sixth District

Amos, James R.	N.D. State Health Dept., Bismarck
Anderson F. E.	Underwood
Arneson, Charles A.	405½ Broadway, Bismarck
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Baumgartner, Carl J.	Quain & Ramstad Clinic, Bismarck
Berg, H. Milton	Quain & Ramstad Clinic, Bismarck
Berg, Roger M.	Quain & Ramstad Clinic, Bismarck
Bertheau, Herman J.	Linton
Boerth, Edwin H.	Workmen's Compensation Bureau, Bismarck
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Carlson, Haakon P.	Hazen

Cartwright, John T.	Missouri Valley Clinic, Bismarck
Cleary, Joseph W.	Missouri Valley Clinic, Bismarck
Curiskis, A. A.	Elgin
Dahl, Phillip O.	Missouri Valley Clinic, Bismarck
Daniolos, Demetrios P.	Quain & Ramstad Clinic, Bismarck
Diven, Wilbur L.	402½ Main, Bismarck
Dunnigan, Ralph J.	Capital City Clinic, Bismarck
Eriksen, Johan A.	St. Alexius Hospital, Bismarck
Ewert, Arthur O.	Beulah
Fardal, Richard W.	Quain & Ramstad Clinic, Bismarck
Fischer, Gerhard	Quain & Ramstad Clinic, Bismarck
Fischer, Hans H.	Quain & Ramstad Clinic, Bismarck
Fleck, Roland	Ashley
Fortman, Albert H., Jr.	Capital City Clinic, Bismarck
Frankel, John B.	Quain & Ramstad Clinic, Bismarck
Freise, Paul W.	Quain & Ramstad Clinic, Bismarck
Fricke, Roger W.	Quain & Ramstad Clinic, Bismarck
Gaebe, Otto C.	1215 No. Mandan St., Bismarck
Garrett, W. G.	Missouri Valley Clinic, Bismarck
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Gonzalez, Gilberto	Missouri Valley Clinic, Bismarck
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Goughnour, Myron W.	Capital City Clinic, Bismarck
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Imes, Seward K.	Quain & Ramstad Clinic, Bismarck
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Johnson, George M.	Missouri Valley Clinic, Bismarck
Johnson, Kenneth J.	Quain & Ramstad Clinic, Bismarck
Johnson, Marlin J. E.	Quain & Ramstad Clinic, Bismarck
Johnson, Paul L.	Quain & Ramstad Clinic, Bismarck
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Kling, Robert R.	Quain & Ramstad Clinic, Bismarck
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Kuplis, Haralds	Turtle Lake
Larson, Leonard W.	Quain & Ramstad Clinic, Bismarck
Lindelow, Olaf V.	Missouri Valley Clinic, Bismarck
Lommen, M. A. K.	Capital City Clinic, Bismarck
Lorenzen, F. C.	Carson
Milligan, Shelagh M.	Medical Arts Center, Mandan
Montz, Charles R.	Quain & Ramstad Clinic, Bismarck
Moreland, J. Wilbur	903 Crescent Lane, Bismarck
Moses, James J.	Quain & Ramstad Clinic, Bismarck
Nuessle, R. F.	Quain & Ramstad Clinic, Bismarck
Oien, Dale R.	Quain & Ramstad Clinic, Bismarck
Orchard, Welland J.	Linton
Owens, Percy L.	State Health Dept., Bismarck
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Peters, Clifford H.	Quain & Ramstad Clinic, Bismarck
Peterson, Alice H.	State Health Dept., Bismarck
Pfeifle, Delano M.	Quain & Ramstad Clinic, Bismarck
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Pitcher, Wayne H.	Quain & Ramstad Clinic, Bismarck
Ramos, Pablo	Quain & Ramstad Clinic, Bismarck
Riecke, Wm. C.	Quain & Ramstad Clinic, Bismarck
Samuelson, Albert F.	Cowan Bldg., Bismarck
Sauer, John P.	Missouri Valley Clinic, Bismarck
Saxvik, Russell O.	Quain & Ramstad Clinic, Bismarck
Schoregge, Robert D.	Quain & Ramstad Clinic, Bismarck
Smeenk, H. Pieter	Quain & Ramstad Clinic, Bismarck
Smith, Clyde L.	Missouri Valley Clinic, Bismarck
Spielman, George H.	Anoka, Minnesota
Tarnasky, Ralph E.	St. Alexius Hospital, Bismarck
Thakor, S. J.	405 E. Broadway, Bismarck
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Tudor, Robert B.	Quain & Ramstad Clinic, Bismarck
Turnacioglu, Omer F.	Quain & Ramstad Clinic, Bismarck
VanVranken, Arthur E.	Quain & Ramstad Clinic, Bismarck
Vinje, Edmund G.	Hazen Clinic, Hazen
Vinje, Ralph	405 E. Broadway, Bismarck
Waldschmidt, Wm. D.	Quain & Ramstad Clinic, Bismarck
Zukowsky, Anthony	Ozone Bldg., Steele

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Carbone, Hubert A.	State Hospital, Jamestown
Chiu, F. Luke	State Hospital, Jamestown
Clement, Duane	320 1st Avenue North, Jamestown
Cukurs, Paul	State Hospital, Jamestown
Curtis, Philip B.	Medical Arts Clinic, Jamestown
Elsworth, John N.	DePuy-Sorkness Clinic, Jamestown
Engberg, Roger D.	DePuy-Sorkness Clinic, Jamestown
Erickson, Oswald P.	State Hospital, Jamestown
Fergusson, Victor D.	Edgeley
Gronewald, Tula W.	State Hospital, Jamestown
Hieb, Edwin O.	DePuy-Sorkness Clinic, Jamestown
Hill, Wayne A.	Kulm
Hogan, Clifford W.	DePuy-Sorkness Clinic, Jamestown
Jansonius, J. W.	Medical Arts Clinic, Jamestown
Larson, Ernest J.	DePuy-Sorkness Clinic, Jamestown
Lucy, Robert E.	DePuy-Sorkness Clinic, Jamestown
March, Bernard W.	State Hospital, Jamestown
Martin, Clarence S.	Medina
Melzer, Simon W.	Woodworth
Miles, James V., Jr.	1209 5th Ave. S.E., Jamestown
Nierling, Richard D.	DePuy-Sorkness Clinic, Jamestown
Oster, Ellis	2119 Sherman Ave., Salt Lake City, Utah
Pederson, T. E.	DePuy-Sorkness Clinic, Jamestown
Sorkness, Joseph	DePuy-Sorkness Clinic, Jamestown
Swafford, Gerald R.	DePuy-Sorkness Clinic, Jamestown
Swenson, John A.	DePuy-Sorkness Clinic, Jamestown
Turner, Neville W.	885 Longview Road, Hillsborough, Calif.
Van der Linde, John M.	Medical Arts Clinic, Jamestown
Van Houten, Richard W.	Oakes
Woodward, Robert S.	DePuy-Sorkness Clinic, Jamestown

Eighth District

Borrud, Chester C.	Harmon Park Clinic, Williston
Craven, John P.	Craven-Hagan Clinic, Williston
Craven, Joseph D.	Craven-Hagan Clinic, Williston
Ellis, Gordon E.	Harmon Park Clinic, Williston
Fennell, William L.	Crosby Clinic, Crosby
Hagan, Edward J.	Craven-Hagan Clinic, Williston
Harvey, Eoin S.	Tioga
Jamieson, John	Tioga
Johnson, Alan K.	Williston Clinic, Williston

Jun, Channing S.	Crosby Clinic, Crosby
Koch, Robert C.	Craven-Hagan Clinic, Williston
Lund, Carroll M.	Williston Clinic, Williston
McCoy, F. E.	107 E. 18th Street, Williston
McPhail, Clayton O.	Crosby Clinic, Crosby
Oliver, Donald C.	Watford City
Olson, M. Jerome	Williston Clinic, Williston
Olson, Robert J.	1504 E. Hillcourt, Williston
Skjei, Donald E.	Williston Clinic, Williston
Strinden, Dean R.	Harmon Park Clinic, Williston
Wiederanders, R. E.	Harmon Park Clinic, Williston
Wright, Willard A.	Williston Clinic, Williston

Ninth District

Ahlness, Paul	Bowman
Bush, Clarence A.	Beach
Dukart, Ralph J.	Dickinson Clinic, Dickinson
Foster, Keith G.	Rodgers-Gumper Clinic, Dickinson
Gilliland, Robert F.	Dickinson Clinic, Dickinson
Gilsdorf, Amos R.	Dickinson Clinic, Dickinson
Guloien, Hans E.	Dickinson Clinic, Dickinson
Gumper, Arnold J.	Rodgers-Gumper Clinic, Dickinson
Hanewald, Walter C.	Rodgers-Gumper Clinic, Dickinson
Hankins, Robert E.	Mott
Hill, S. W.	Regent
Lara, Henry R. C.	St. Joseph's Hospital, Dickinson
Larsen, Harlan C.	Rodgers-Gumper Clinic, Dickinson
Lorentzen, Donald E.	Hettinger
Maercklein, Otto C.	Mott
Nicely, Donald A.	Rodgers-Gumper Clinic, Dickinson
Ordahl, Norman B.	Rodgers-Gumper Clinic, Dickinson
Raasch, Richard F.	30 West 8th Street, Dickinson
Reichert, Donald J.	24 West Villard, Dickinson
Reichert, H. Lawrence	24 West Villard, Dickinson
Retzer, Paul G.	Hettinger
Sailer, Gerald T.	Hettinger
Sawchuk, Andrew C.	Dickinson Clinic, Dickinson
Skwarok, Walter S.	Hebron
Slominski, Henry	Richardton
Smith, Oscar M.	P.O. Box 1188, Dickinson
Spear, Albert E.	610 1st Avenue W., Dickinson
Thom, Robert C.	Bowman
Wolf, Dennis E.	Richardton

Tenth District

Breen, Donald J.	Hillsboro
Hlavinka, Delbert J.	Mayville
Kloster, Ronald M.	Mayville
LaFleur, Harold A.	Mayville
Little, James M.	Mayville
Little, Roy C.	Mayville
McLean, Robert W.	Hillsboro
Oja, Karl F.	Portland
Patton, Peter W. S.	Cooperstown
Wakefield, Kenneth M.	Cooperstown

Ovulen® as an Oral Contraceptive—Edward A. Banner, M.D.

(Continued from page 465)

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Open (Retropubic) Prostatectomy—Riba, Mehn, Logan, and Borkovec, M.D.s

(Continued from page 470)

fifteen months). They have been due to vesical neck fibrosis (10 or 4.6%), incomplete or recurrent adenoma (6 or 2.7%), muscular hypertrophy (8 or 3.7%) (Fig. 11), and residual carcinoma in the prostatic capsule (4 or 1.9%).

The routine use of antibiotics controls the operative and postoperative sepsis. Hemorrhage, the remaining major complication, can be minimized by careful precautions and hemostasis at the time of surgery. Scrotal or intrapelvic vasectomies prevent epididymitis. Simultaneous hernial repairs are feasible, economical, and add additional comfort to the postoperative patient.

REFERENCES

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News Briefs . . .

North Dakota

DR. HERBERT G. KUNKEL has started practice in Grand Forks as an anesthesiologist. He formerly practiced in Aliquippa, Pa.

* * * *

DR. JOHN A. SWENSON has returned to the DePuy-Sorkness Clinic in Jamestown after completing a fellowship in internal medicine at the University of Minnesota.

* * * *

DR. JOSEPH E. ADDUCCI, an obstetrician and gynecologist, has joined the Craven-Hagan Clinic in Williston. Dr. Adducci completed his active duty in the U.S. Army in June.

* * * *

DR. WILLIAM M. GOODALL has started practice in association with Dr. Nicholas Kaluzniak of Langdon. Dr. Goodall recently completed his internship at the Winnipeg General Hospital, Winnipeg, Canada.

* * * *

DR. ROBERT W. SPLETTSTOESSER, an internist, has opened a practice in Ashley in association with Dr. Roland Fleck at the Ashley Clinic. Dr. Splettstoesser formerly practiced in Belle Plaine, Minn.

* * * *

DR. HUBERT A. CARBONE, psychiatrist and superintendent of the State Hospital at Jamestown, has been appointed director of the Mental Health and Retardation Division of the State Health Department.

* * * *

DR. DAVID C. SMISSON, Augusta, Ga., has begun an association with Dr. Guenther H. Heidorn at the Main Medical Building in Minot. Dr. Smisson is a specialist in internal medicine and cardiology.

Minnesota

DR. LAWRENCE J. LEONARD of Minneapolis is one of ten Minnesota doctors who received special citations for fifty years of medical practice. The citation was given to Dr. Leonard during the annual meeting of the Minnesota State Medical Association in St. Paul, May 16-17.

* * * *

DR. WALTER P. SAVAGE, a psychiatrist, has joined the staff of the Southwestern Mental Health Center in Luverne. Dr. Savage comes from Rockville, Md., where he was

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at the National Institute of Mental Health at Bethesda, Md.

* * * *

DR. DAVID K. MCAFEE, a general surgeon, has joined the staff of the Lakeland Medical Center in Willmar. Dr. McAfee formerly practiced in Miles City, Mont.

* * * *

THE FIRST IN A SERIES of satellite artificial kidney centers will be established at St. Gabriel's Hospital in Little Falls. The center will be an extension of the community artificial kidney center now operating at Hennepin County General Hospital in Minneapolis under the direction of Dr. Fred L. Shapiro.

* * * *

THE RAMSEY COUNTY HEART DIVISION of the Minnesota Heart Association is sponsoring an on-going series of cardiac conference programs which is open to all physicians free of charge. The conferences are being held at Charles T. Miller Hospital in St. Paul every other Wednesday. For more information call the Minnesota Heart Association, 646-6554.

* * * *

DR. ROGER SCHROEPPEL, a recent graduate of the University of Minnesota Medical School, has joined his father, Dr. John E. Schroeppel, in his practice at Winthrop.

* * * *

DR. AHMAD ORANDI, former urologist at St. Luke's Hospital in New York City, has joined the medical staff of Lake Region Hospital in Fergus Falls. He will also maintain offices in the Park Region Clinic and the Fergus Falls Clinic.

* * * *

DR. GERALD T. FRANE has joined Drs. Schissel, Pattee, and Leighton in Crystal. Dr. Frane is a recent graduate of the University of Minnesota Medical School.

* * * *

PRESIDENT O. MEREDITH WILSON of the University of Minnesota has asked legislators for ultimate funds of over $53 million by 1975 to expand the University of Minnesota Medical and Dental Schools. The expansion is intended to increase medical enrollment by 1980 to 250, dental to 200, and other categories similarly. A recent study shows that the shortage of health workers in Minnesota will become worse unless greater numbers are trained each year.

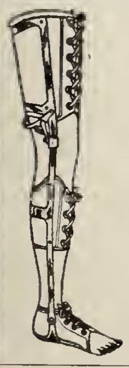
* * * *

DR. RICHARD J. KLINE, who has been a resident in surgery in the Mayo Graduate School of Medicine, Rochester, will be located in Grand Forks, N.D.

* * * *

DR. ELTON WING has joined Dr. Elmer E. Keithahn at Sleepy Eye. Dr. Wing recently completed his internship in St. Paul.

(Continued on page 18A)



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(Continued from page 17A)

South Dakota

DR. BUCK J. WILLIAMS has joined Dr. Milton G. Mutch in the practice of obstetrics and gynecology at Sioux Falls.

* * * *

DR. NATHANIEL R. WHITNEY, JR., of Rapid City, who has served as Pennington County health officer for the past ten years, has resigned effective Sept. 1.

* * * *

DR. DAVID F. PIRO, a surgeon at the U.S. Army hospital at Ft. Ord, Calif., will join the staff of the Bartron Clinic in Watertown.

Deaths . . .

DR. GEORGE B. EUSTERMAN, SR., 84, died July 11 in Rochester. The Mayo Clinic pioneer joined the clinic in 1908 after receiving his medical degree from the University of Minnesota Medical School. When he retired in 1950, he was recognized as one of the world leaders in gastroenterology.

* * * *

DR. GEORGE M. TANGEN, 68, died July 23 in Taylors Falls, Minn. Dr. Tangen was a former associate professor in the Department of Otolaryngology at the University of Minnesota Hospitals. He received his medical degree from the University of Minnesota Medical School in 1925.

* * * *

DR. SIDNEY C. BLACKMORE, 53, of Hoyt Lakes, Minn., died July 3. He was a staff member of the East Range Clinic at Aurora since 1954 and a 1942 graduate of the University of Minnesota Medical School.

* * * *

DR. AND MRS. ROGER A. STANDARD of Aberdeen, S.D., were killed in the crash of their light plane in upper New York state on June 15. Dr. Standard, 52, was an orthopedic surgeon who had practiced in Aberdeen since 1961 after retiring from the Navy Medical Corps. He received his medical degree in 1941 from the Loma Linda University School of Medicine, California.

* * * *

DR. CHARLES R. SULLIVAN, 45, died July 3 at Augusta, Ga. Dr. Sullivan was a member of the Section of Orthopedic Surgery of the Mayo Clinic from 1955 to 1966 and former assistant professor of orthopedic surgery in the Mayo Graduate School of Medicine, University of Minnesota at Rochester. In 1966, Dr. Sullivan left the Mayo Clinic to become a member of the faculty of the Medical College of Georgia at Augusta. He received his medical degree from the University of Rochester School of Medicine and Dentistry in 1946.

* * * *

DR. WILLIAM DUNCAN, 60, of Webster, S.D., died June 9. Dr. Duncan had practiced in Webster for thirty-five years and was a past president of the state medical association. He received his medical degree from the University of Minnesota Medical School in 1929.

* * * *

DR. FRITZ B. SCHLEINITZ, 54, died June 12 in Hankinson, N.D. Dr. Schleinitz received his medical degree from the University of Minnesota Medical School in 1936 and had practiced in Hankinson for nineteen years.

Classified Advertisements

GENERAL PRACTITIONER, associate, urgently needed. Unopposed practice established 20 years. 32 bed new hospital with additional 20 bed chronic unit. Good anesthesia coverage, laboratory facilities. Excellent clinic one block from hospital. Salary with early partnership. Locum tenens also considered. Call collect 218-782-4725 or write Klefstad Clinic, Greenbush, Minn.

SACRED HEART, MINNESOTA has been without a doctor since 1961. General practitioner will find suitable building in 700 pop. village, modern hospital 10 miles away; progressive, stable community in west central part of state. Good school, churches. Good family environment. Call or write Rev. Robert Bardy, Telephone 765-2547, Sacred Heart, Minn.

WANTED: GP to join clinic serving population area of 12,000. City has new hospital, new clinic building, two nursing homes, new Jr-Sr high school, new swimming pool, rich farming area in Red River Valley. Fishing and hunting nearby; metropolitan city close by. Salary open and partnership if interested. Write or call Warren Clinic, Warren, Minn. 56762. 742-6231, area code 218.

WANTED: GENERAL PRACTITIONERS and Pediatrician to join expanding Northwestern Wisconsin 8-man group. New clinic building with full facilities; modern hospitals; excellent school system including Wisconsin State University; pop. 34,000; early partnership if compatible. Write or call collect R. L. Larson, Mgr., Superior Clinic, Superior, Wis. Phone 715-392-8111.

RESIDENCIES IN PHYSICAL MEDICINE and rehabilitation offer challenge and opportunity in a growing field. Comprehensive training utilizing Mayo Clinic facilities and faculty, at $3,600 to $10,000 stipend. Attractive community, excellent school system, cultural advantages. Contact Gordon M. Martin, M.D., Mayo Graduate School of Medicine, Rochester, Minnesota 55901.

OPENINGS FOR: Clinic Director, Psychiatrist, $17,500; Clinical Psychologist, $11,500; Psychiatric Social Worker, $9,500. The recently organized, soon to be opened, full-time Massanutten Mental Health Center located in the heart of the beautiful Shenandoah Valley in Harrisonburg, Virginia is now prepared for staffing. Here are unmatched groundfloor opportunities to use your abilities and enjoy life. No professional Psychiatrists practice in the three counties you will serve. You will have the complete support of every medical facility and doctor in this area. By car, Harrisonburg is approximately two hours from Washington, two hours from Richmond, two hours from Roanoke and only one hour from the University Hospital Medical Center in Charlottesville, Virginia. For complete information write or phone: Hallen G. Helbert, M.D., 1031 South Main Street, Harrisonburg, Virginia, Phone 434-8181.

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WANTED—INTERNIST, Board Certified or qualified to associate with 5 doctor clinic. In growing economy of industrial and summer and winter tourist area. Grand Rapids Clinic, 504 1st Ave. N.W., Grand Rapids, Minn. Phone 112-218-326-3426.

WANTED—GENERAL PRACTIONER for Southeast North Dakota community, group affiliation and guarantee available to right man. 100 bed hospital within 15 miles. May reside in larger community and service from there. Formerly served by M.D. Excellent potential and the best of facilities and equipment intact. Write Clarence George, 403 North Seventh Street, Wahpeton, North Dakota.

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CORTENEMA
Hydrocortisone 100 mg
Retention Enema
FOR RECTAL USE ONLY
60 cc.
Caution: Federal law prohibits dispensing without prescription.
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NEW Cortenema™

The first disposable hydrocortisone retention enema specifically for the treatment of ULCERATIVE COLITIS

EFFECTIVE in clinical study of 55 cases[1 2] with varied severity and extent of involvement. Marked clinical improvement was noted within 5-7 days in 90%; proctologic improvement in 94% within 3 weeks. **CORTENEMA** provides both topical and systemic effects because Hydrocortisone Alcohol is absorbed to a significant extent from the colon.

CONVENIENT for both hospital and out-patient use. The standardized, disposable single-dose unit is ready to use, requires no mixing and is simply self-administered.

ECONOMICAL since the average dosage requires only one enema daily for 2 or 3 weeks, then one every other day until remission is established. The selection of Hydrocortisone permits lower patient cost without sacrificing efficacy.

1 Sherman, L. F.: Minnesota Med. 48:605 May, 1965 2 Sherman, L. F. Personal Communication

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Cortenema

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Each 60 cc. unit contains:

Hydrocortisone..100 mg. in aqueous, isotonic saline containing methylcellulose as a suspending agent and emollient, polysorbate 80, and 0.18% methylparaben and 0.02% propylparaben, as preservatives.

Description: CORTENEMA Hydrocortisone Retention Enema is a completely disposable, single-dose unit consisting of a flexible plastic container with a lubricated applicator tip for rectal administration. It is designed to permit self-administration and, therefore, it is suitable for both out-patient and hospital use. It also may be diluted with isotonic saline for administration by intrarectal drip.

CORTENEMA consists of a suspension of partially solubilized hydrocortisone alcohol in an aqueous vehicle. Thus, it provides the potent anti-inflammatory effect characteristic of the corticosteroids. Because hydrocortisone alcohol is absorbed to some extent from the colon, CORTENEMA provides both topical and systemic actions.

Indications: CORTENEMA Hydrocortisone Retention Enema is indicated as an adjunct in the treatment of idiopathic nonspecific ulcerative colitis. It is most useful in cases involving the rectum, sigmoid and left colon, where it exerts a topical effect. Due to its systemic action, CORTENEMA has proved effective in certain cases extending to the transverse and ascending colons.

Rectal steroid therapy brings about prompt symptomatic and proctologic remissions in a significant proportion of patients, but it apparently does not alter the recurrent and progressive nature of ulcerative colitis. Therefore, this form of treatment is not recommended for prophylaxis during periods of remission.

Contraindications: Local contraindications to the use of intrarectal steroids include obstruction, abscess, perforation, peritonitis, fresh intestinal anastomoses, extensive fistulas and sinus tracts. Tuberculosis (active, latent or questionably healed), ocular herpes simplex, and acute psychosis are usually considered absolute contraindications to the use of corticosteroids.

Relative contraindications include active peptic ulcer, acute glomerulonephritis, myasthenia gravis, osteoporosis, diverticulitis, thrombophlebitis, psychic disturbances, pregnancy, diabetes, hyperthyroidism, acute coronary disease, hypertension, limited cardiac reserve, and local or systemic infections, including fungal or exanthematous diseases. Where these conditions exist, the expected benefits from CORTENEMA must be weighed against the risks involved in its use.

If clinical or proctologic improvement does not occur within two or three weeks after starting CORTENEMA, discontinue its use.

Precautions: CORTENEMA Hydrocortisone Retention Enema should be administered with caution in patients with severe ulcerative disease because these patients are predisposed to perforation of the bowel wall. In the advanced stages of chronic ulcerative colitis, where there is loss of mucosa, and thickening and fibrosis of the bowel wall, steroid therapy theoretically might hasten deterioration, although this has not been proved with steroids in actual practice.

In severe cases, where surgery is imminent in the absence of marked clinical improvement, it is hazardous to wait more than a few days for a satisfactory response to medical treatment.

Because of the possibility of adrenal insufficiency caused by suppression of the adrenal cortex by glucocorticoids especially after prolonged therapy, it is important that therapy be withdrawn gradually. If the patient is subjected to unusual stress, while on therapy or up to a year after discontinuation of steroids, adequate supportive measures and increased or reinstated systemic steroid therapy are indicated. In the case of surgery, these measures should be continued throughout the pre- and postoperative recovery periods, bearing in mind the possible deleterious effects of corticosteroids on fresh intestinal anastomoses.

Steroid therapy might impair prognosis in surgery by increasing the hazard of infection. If infection is suspected, appropriate antibiotic therapy must be administered, usually in larger than ordinary doses.

General precautions common to all corticosteroid therapy should be observed during treatment with CORTENEMA, including those pertaining to growth suppression in children during prolonged use. Patients should be kept under close observation. If severe reactions or idiosyncrasies occur, steroids should be discontinued immediately and appropriate measures instituted.

If it is necessary to use CORTENEMA in pregnant patients, their infants should be closely observed for signs of hypoadrenalism; and appropriate measures, including administration of corticosteroids, should be instituted if such signs are seen.

HYDROCORTISONE RETENTION ENEMA DISPOSABLE UNIT

FOR RECTAL USE ONLY

Adverse Reactions: CORTENEMA Hydrocortisone Retention Enema may produce all of the side effects known to occur with other forms of hydrocortisone therapy. These include moon face, buffalo hump, fluid retention, excessive appetite and weight gain, abnormal fat deposits, mental symptoms, hypertrichosis, acne, striae, ecchymosis, increased sweating, pigmentation, dry scaly skin, thinning scalp hair, thrombophlebitis, decreased resistance to infection, negative nitrogen balance with delayed bone and wound healing, menstrual disorders, neuropathy, peptic ulcer, decreased glucose tolerance, hypopotassemia, adrenal insufficiency, necrotizing angiitis, hypertension, pancreatitis and increased intraocular pressure.

In children, suppression of growth may occur. Increased intracranial pressure may occur and possibly account for headache, insomnia and fatigue. Subcapsular cataracts may result from prolonged usage. Long-term use of all corticosteroids results in catabolic effects characterized by negative protein and calcium balance. Osteoporosis, spontaneous fractures and aseptic necrosis of the hip and humerus may occur as part of this catabolic phenomenon.

Where hypopotassemia and the other symptoms associated with fluid and electrolyte imbalance call for potassium supplementation and salt-poor or salt-free diets, these may be instituted and are compatible with the diet requirements for ulcerative colitis.

Dosage and Administration: The use of CORTENEMA Hydrocortisone Retention Enema as an adjunct in the treatment of ulcerative colitis is predicated upon the concomitant use of modern supportive measures, such as blood replacement, rational dietary control, antispasmodics and sedatives, antibacterial therapy, and systemic steroids.

The usual dose is one CORTENEMA Hydrocortisone Retention Enema daily for two or three weeks and every second day thereafter, administered intrarectally in the evening before retiring. Every effort should be made to retain the medication for at least one hour, preferably all night. This may be facilitated by prior sedation and or antidiarrheal medication. If clinical or proctologic improvement fail to occur within two or three weeks, discontinue the drug.

For administration by retention enema, instruct the patient to lie on his left side during instillation. Shake the bottle vigorously to resuspend the insoluble portion of hydrocortisone. Expose the lubricated tip by removal of the protective sheath, grasping the bottle at the neck where it is most rigid. Carefully insert the lubricated tip into the rectum in the direction of the sacrum. Slowly express the contents by compressing the container. After instillation, the patient should remain on his left side for at least 30 minutes, to allow distribution of the medication throughout the descending colon and rectum.

For coverage of more distant segments of the colon, CORTENEMA Hydrocortisone Retention Enema may be diluted to from 100 cc. to 300 cc. with isotonic saline and administered by intrarectal drip.

The duration of treatment is dependent on the degree of response. If a satisfactory response is to be obtained, it usually occurs within five to seven days, as evidenced by a marked reduction of clinical symptoms. Improvement in the appearance of the mucosa, gauged by barium enemas and sigmoidoscopic examinations, may lag somewhat behind clinical improvement. The usual duration of therapy is two weeks, although some cases require therapy for longer periods (up to two or three months). Minimal control of symptoms is an insufficient basis for the prolonged use of CORTENEMA. If there is no clinical or proctologic response within two or three weeks, or if the patient's condition worsens, discontinue the drug.

Because of hydrocortisone absorption, proper precautions against unwanted systemic reactions or side effects should be observed. Symptomatic improvement, evidenced by decreased diarrhea, weight gain, improved appetite, lessened fever, and decrease in leukocytosis, may be misleading and should not be used as the sole criterion in judging efficacy. Actual sigmoidoscopic examination and X-ray visualization are most reliable. Since steroids can inhibit wound healing, enema or drip therapy should not be employed in the immediate or early postoperative period following ileorectostomy.

How Supplied: CORTENEMA Hydrocortisone Retention Enema is supplied in boxes of seven single-dose units.

Caution: Federal law prohibits dispensing without a prescription.

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For peptic ulcer, gastric hyperacidity, gastritis

Each WinGel tablet or teaspoon (5 ml.) contains 410 mg. of combined, highly reactive, short polymer, aluminum and magnesium hydroxides **stabilized with hexitol.**

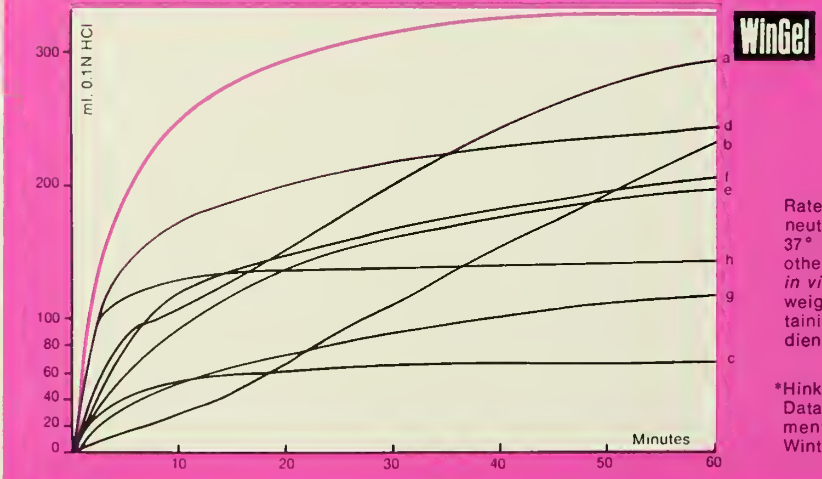
Neutralizes 300 times its active-ingredient weight in gastric acid for fast, long-lasting relief

Gastric or duodenal ulcer, acute or chronic gastritis, gastric hyperacidity...wherever there is "acid overflow" new WinGel can provide faster, longer, more complete neutralization.

In recent laboratory comparisons* with eight other leading antacids, new WinGel tablets not only neutralized more hydrochloric acid per active-ingredient weight, but neutralized it faster and longer than all other antacids tested.

Pleasant pink in color, WinGel is delicately mint flavored with a smooth-as-cream texture—qualities sure to please the patient on long-term therapy. New WinGel is also specially formulated to avoid constipation or diarrhea.

New WinGel neutralizes 300 times its active-ingredient weight in 0.1N hydrochloric acid—neutralizes more acid faster than other leading antacids



Rate of 0.1N hydrochloric acid neutralization at pH 3.5 and 37° with WinGel and eight other leading antacid tablets—*in vitro*. Samples equaled the weight of tablet material containing 1.0 Gm. active ingredients.*

*Hinkel, E. T., Jr. (New York): Data in the files of the Department of Medical Research, Winthrop Laboratories.

Dosage: Peptic ulcer or gastritis—from 2 to 4 teaspoons of WinGel liquid or 2 to 4 tablets chewed or allowed to dissolve in the mouth every two to four hours. **Gastric hyperacidity**—2 tablets or teaspoons about ½ to one hour after meals as needed; children from 7 to 14 years of age, 1 or 2 tablets or 1 or 2 teaspoons of liquid as needed.

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OCTOBER 1966

Rowell responds to the 'cold' patient's comprehensive problem with the 'total therapy' concept

Colrex Compound

PHENYLEPHRINE TO RELIEVE NASAL CONGESTION with a potent vaso-constrictor that does not lead to "rebound congestion."

CHLORPHENIRAMINE TO COMBAT EXCESSIVE SECRETION without causing excessive drying of the delicate nasal mucosa.

CODEINE TO SUBDUE COUGH remains the best antitussive and appears to act synergistically with PAPAVERINE in the relief of cold symptoms—and to enhance aspirin analgesia.

ALUMINUM ASPIRIN TO REDUCE FEVER AND ACHE with less possibility of salicylate-induced gastric upset. PLUS VITAMIN C TO HELP MAINTAIN CAPILLARY INTEGRITY.

NEGLECTS NO ASPECT OF THE RESPIRATORY SYNDROME

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EACH CAPSULE CONTAINS:

Codeine phosphate	16 mg.
(Warning: May be habit-forming)	
Papaverine hydrochloride	16 mg.
Aluminum aspirin	300 mg.
Phenylephrine hydrochloride	5 mg.
Chlorpheniramine maleate	2 mg.
Vitamin C	100 mg.

Dosage: Adults, 1 capsule 3 or 4 times daily; children, according to age and weight.

Indications: Cough, congestion, headache, discomfort and muscular aches and pains in coryza, rhinitis, sinusitis, pharyngitis, laryngitis, tracheitis, bronchitis, grippe, influenza and pneumonia.

Side effects and precautions: Side effects are infrequently encountered. Codeine and aluminum aspirin should not be given to patients with known idiosyncrasies to these drugs. Antihistaminic agents may cause drowsiness in susceptible individuals. Colrex Compound should be used with caution in hypertensive patients.

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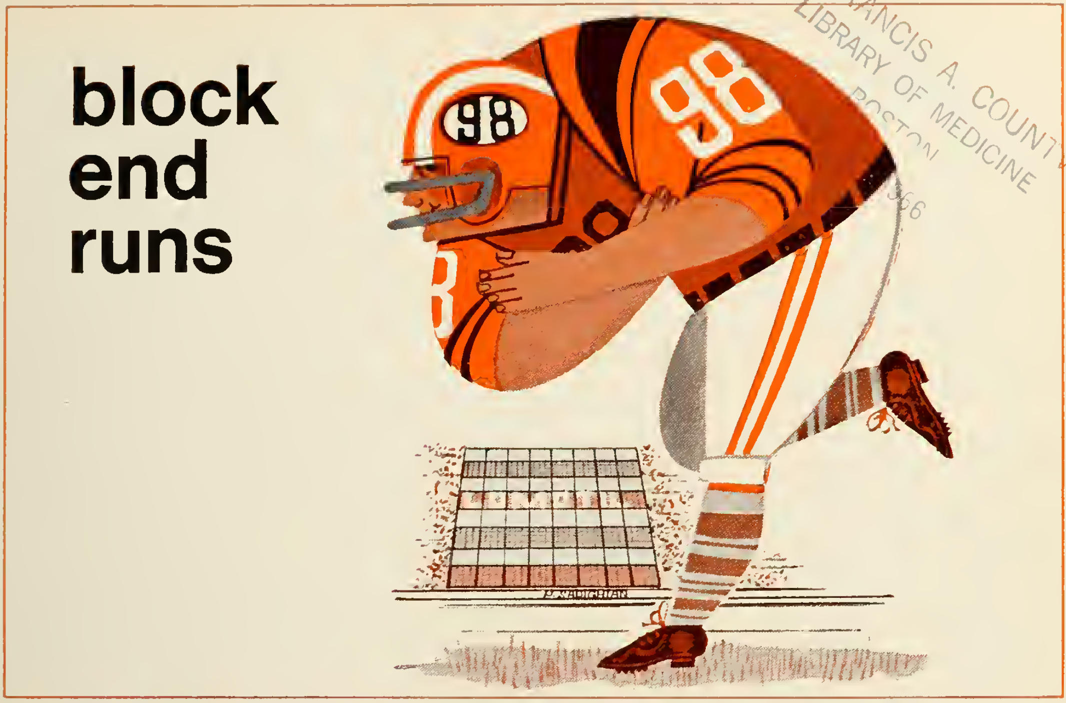

LOMOTIL® tablets liquid

Each tablet and each 5 cc. of liquid contains:

diphenoxylate hydrochloride . . . . (Warning: May be habit forming)	2.5 mg.
atropine sulfate	0.025 mg.

tackles the problem of diarrhea directly

Effectiveness—Physiologic evidence indicates that Lomotil acts directly on the smooth muscle of the bowel to lower motility and control diarrhea. This action is unsurpassed in promptness and efficiency.

Convenience—Lomotil is available as small, easily carried, virtually tasteless tablets and as a pleasant, fruit-flavored liquid.

Versatility—The therapeutic efficiency, safety and convenience of Lomotil may be used to advantage alone or adjunctively in diarrhea associated with:

- Functional hypermotility
- Irritable bowel
- Acute infections
- Gastroenteritis and colitis
- Malabsorption syndrome
- Regional enteritis
- Ileostomy
- Ulcerative colitis
- Food poisoning
- Drug therapy

For correct therapeutic effect
Rx correct therapeutic dosage

Dosage: The recommended initial daily dosages, given in divided doses until diarrhea is controlled, are:

Children: Total Daily Dosage

3-6 mo. . .	½ tsp.* t.i.d. (3 mg.)
6-12 mo. .	½ tsp. q.i.d. (4 mg.)
1-2 yr. . . .	½ tsp. 5 times daily (5 mg.)
2-5 yr. . . .	1 tsp. t.i.d. (6 mg.)
5-8 yr. . . .	1 tsp. q.i.d. (8 mg.)
8-12 yr. . .	1 tsp. 5 times daily (10 mg.)
Adults: . .	2 tsp. 5 times daily (20 mg.) (or 2 tablets q.i.d.)

*Based on 4 cc. per teaspoonful.

Maintenance dosage may be as low as one-fourth the initial daily dosage.

Precautions: Lomotil, brand of diphenoxylate hydrochloride with atropine sulfate, is a Federally exempt narcotic preparation of very low addictive potential. Lomotil should be kept out of reach of children since accidental overdosage may cause severe respiratory depression. Recommended dosages should not be exceeded. Lomotil should be used with caution in patients with impaired liver function and in patients taking addicting drugs or barbiturates. The subtherapeutic amount of atropine is added to discourage deliberate overdosage.

Side Effects: Side effects are relatively uncommon but among those reported are gastrointestinal irritation, sedation, dizziness, cutaneous manifestations, restlessness, insomnia, numbness of extremities, headache, blurring of vision, swelling of the gums, euphoria, depression and general malaise.

SEARLE *Research in the Service of Medicine*

The Journal-Lancet

Volume 86, No. 10, OCTOBER 1966

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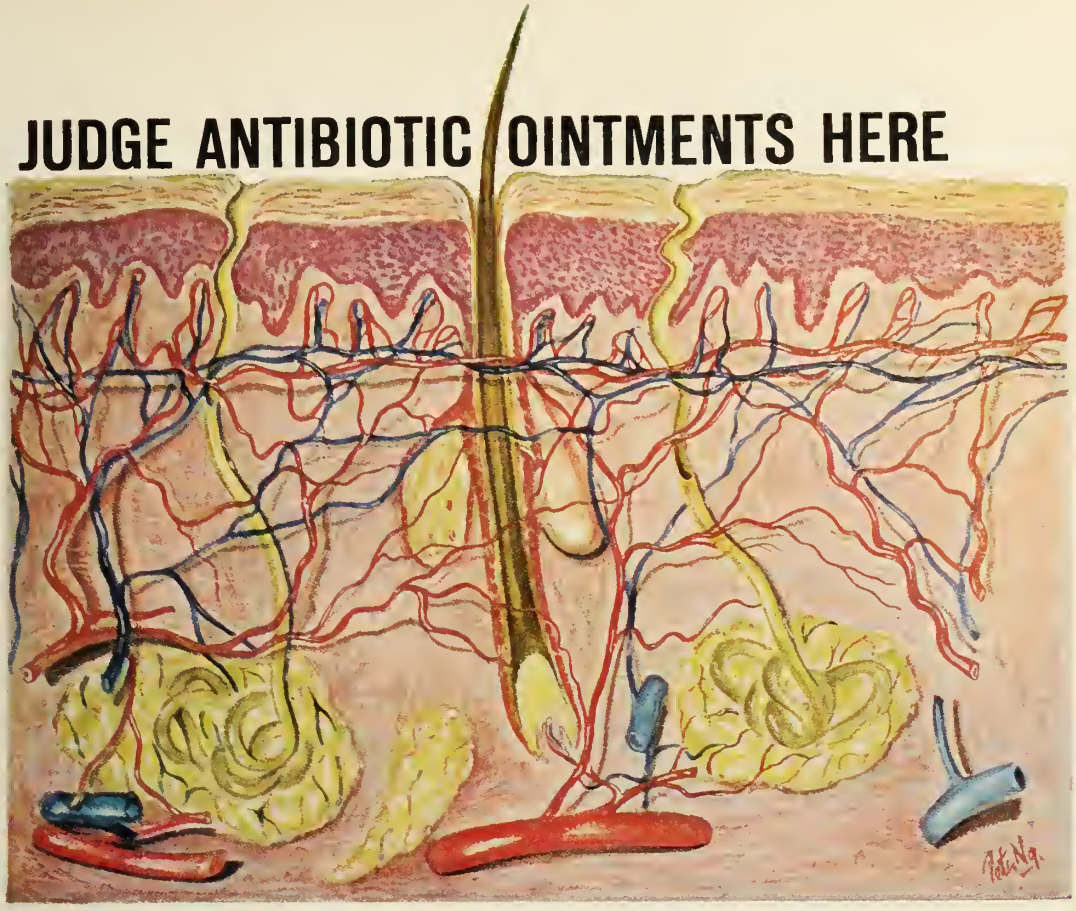

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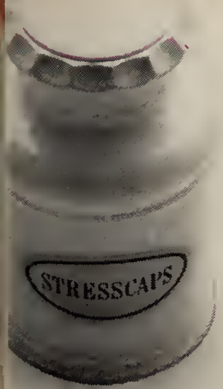

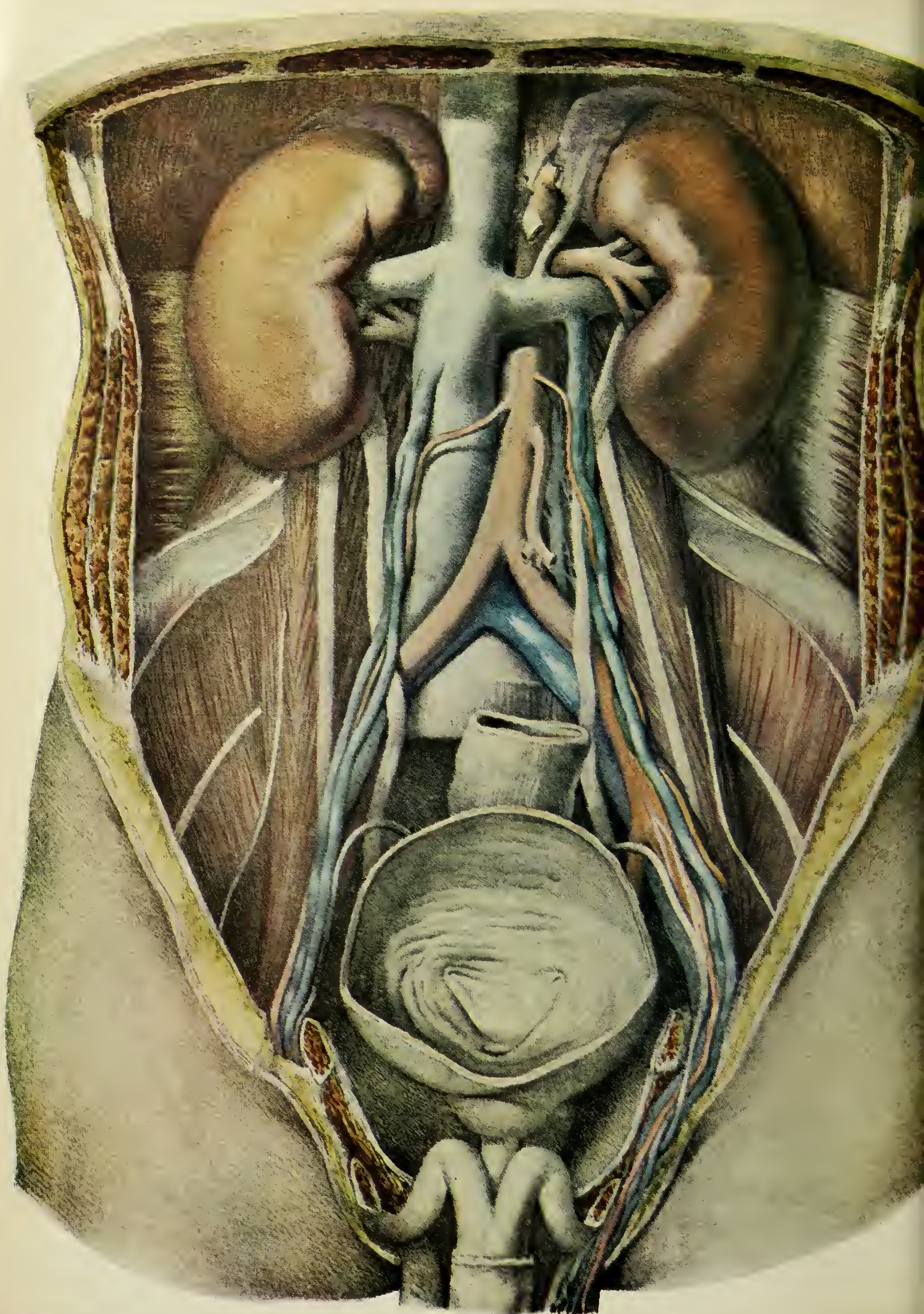

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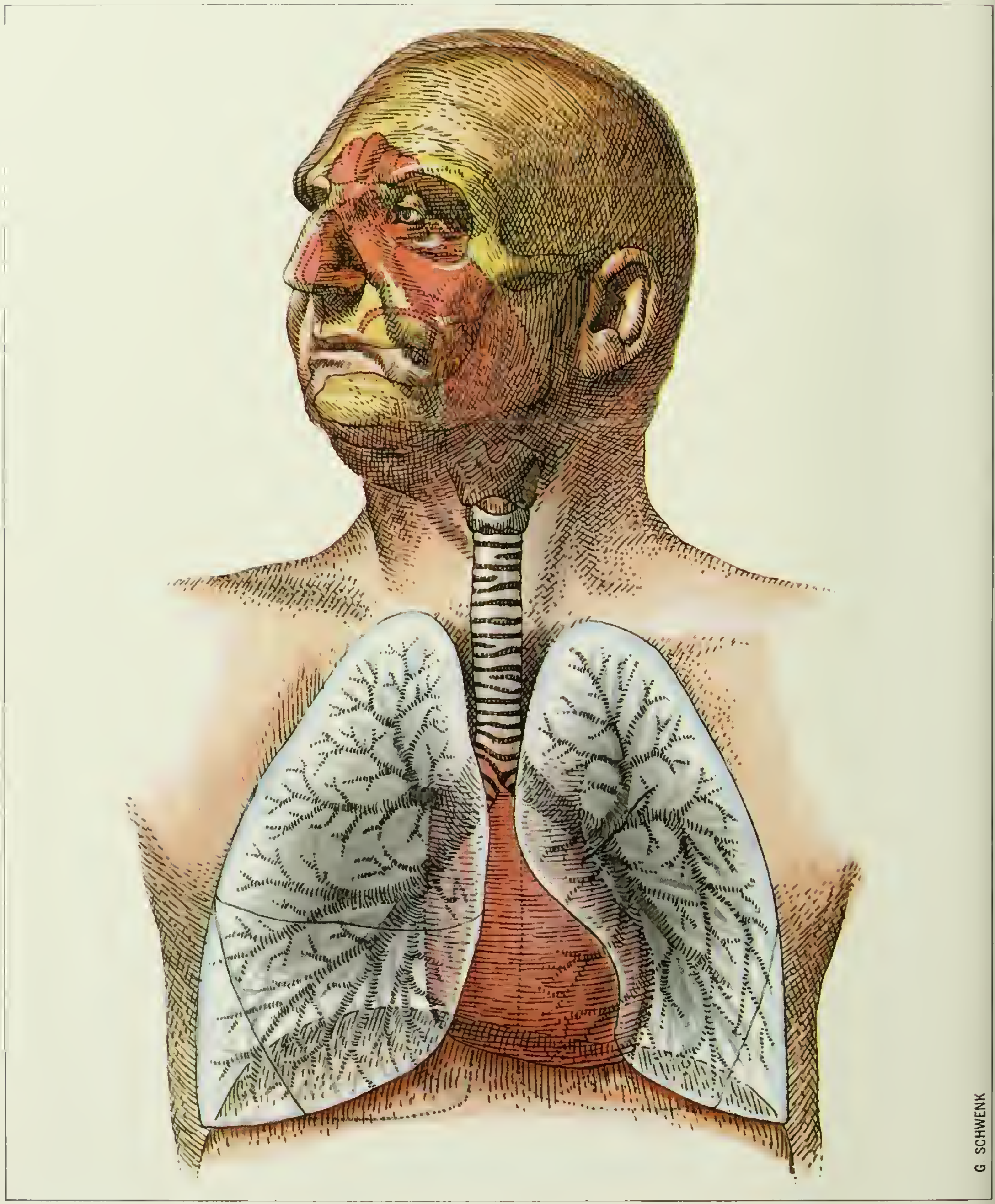
this issue: the common cold and the aging patient

the common cold and the aging patient

Louis J. Vorhaus, II, M.D., F.A.C.P.



Effects of aging on the anatomic and physiologic aspects of the respiratory apparatus.

The chest becomes more fixed, less mobile and less elastic as the bronchial walls and thoracic ligaments lose elasticity. The diaphragm and intercostal muscles atrophy and weaken. The lungs become smaller, flabbier and weigh less, decreasing vital and total lung capacity, increasing residual volume and the alveolar dead space.

Sir William Osler described pneumonia as the welcome friend of the aged patient, because the patient with pneumonia usually died quietly. But today, the well-informed physician is an even better friend of the aging patient, since it is better to live than to die, no matter how quietly.

One of the first avenues of approach in the control of the hazards of respiratory disease in the aging patient is prompt and proper attention to the common cold or upper respiratory infection. The common cold may be the first step in the relatively short path to lower respiratory infection, broncho-pneumonia and death. This train of events occurs frequently among older persons. Indeed, pneumonia is one of the most common causes of their admission to hospitals and ranks high on the list of geriatric killers. Colds are more debilitating in elderly people and the aged are more likely candidates for secondary infections such as sinusitis and bronchitis. These infections, in turn, are more prone to lead to bronchopneumonia, because of lowered resistance and anatomic and physiologic changes in the lungs of the elderly.

What is different about the respiratory tree of an aged person and that of an otherwise healthy younger adult? Aging certainly takes its toll on all parts of the body, affecting both anatomic and physiologic aspects of the respiratory apparatus. These changes are in part due to the wear and tear that occurs over the years; the repeated bouts of respiratory infection, long exposure to atmospheric pollutants, to occupational inhalants, smoking, malnutrition, obesity, inactivity and the development of other diseases which may affect the lungs.

With the passage of years, the lungs change. They become scarred and emphysematous and lose their compliance. The whole chest becomes more fixed, less mobile and less elastic.

the anatomic changes that occur in aging render the lungs less efficient. Tests of pulmonary function in senescence show a deterioration characterized by a decrease in vital capacity and total lung capacity, an increase in residual volume and alveolar dead space. Maximum breathing capacity is reduced and uniformity of ventilation deteriorates. These problems are often aggravated by the obstructed breathing, fever and secondary infection associated with the common cold, placing an additional stress on the entire cardiopulmonary reserve.

In addition, the efficiency of a cough is below par in older persons even though they are in good health. This is partly due to the decreased respiratory excursions and distensibility of the chest wall, and partly from loss of elasticity of bronchial walls which tend to make them collapse in a cough.

The elderly patient's resistance to infection is often reduced. Nutritional deficiencies are more common in aged people. There is some evidence to indicate that their capacity to respond to stress is less efficient. Finally, there is often relatively meager symptomatic response to acute disease. The absence of obvious or dramatic clinical signs and symptoms of severe illness is particularly dangerous because, coming as it

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does in a person whose defenses are weakened both locally and systemically, pulmonary disease may progress rapidly to irreversible stages before medical attention is sought. Respiratory infection is especially hazardous because the aged patient responds badly to hypoxia. Not only is his response to oxygen lack impaired, but the work of breathing, due to decreased compliance of the lung and increased stiffness of the thorax, is markedly augmented.

Many patients late in life are in a precarious and delicate cardiopulmonary balance which is easily decompensated from relatively minor insults such as colds and upper respiratory infections.

For all of these reasons, geriatricians long have stressed the importance of preventing respiratory insults. Today we have better ways of treating respiratory infection, improved techniques for clearing the lungs and bronchial tubes of secretions and better understanding of ways of improving ventilation. We possess a broader spectrum of antimicrobial agents including newer ones to deal with previously resistant organisms. Even so, the death rate from pneumonia is high in older people, and it is preferable to avoid the disease than to treat it. To do so, attention must be paid to the general maintenance of good health and all that implies, as well as to the prevention, elimination and treatment of associated conditions that predispose to or cause pneumonia such as chronic upper or lower respiratory infection, respiratory allergy, chronic sinusitis and exposure to inspired irritants.

Colds and other minor respiratory infections, which favor the development of broncho-pneumonia, should be treated vigorously and promptly, particularly those patients whose aging process has been accompanied by the development of chronic pulmonary disease. Upper respiratory passages should be cleared with decongestants. Sinuses should be drained adequately. And, when indicated, appropriate antimicrobial therapy should be instituted before serious infection of the lower respiratory tree supervenes.

In decades past it was understandable that physicians welcomed pneumonia for the aged patients because it offered them a quiet and peaceful demise. Today we recognize that in many cases, peaceful as it may have been, such deaths were often avoidable. With the current knowledge and understanding of the problems that respiratory infections impose on aging people, vigilant medical attention can often restore them to a vigorous, rewarding and productive life so that the many opportunities that exist today for people to enjoy their golden years are realized and not stolen by untimely death.

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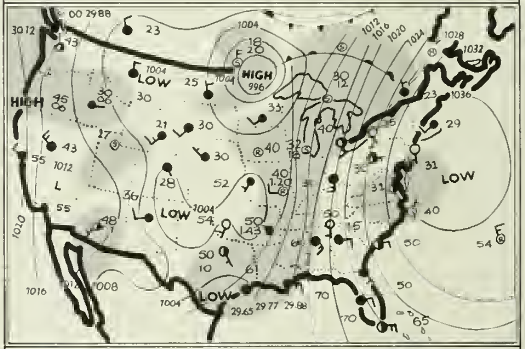

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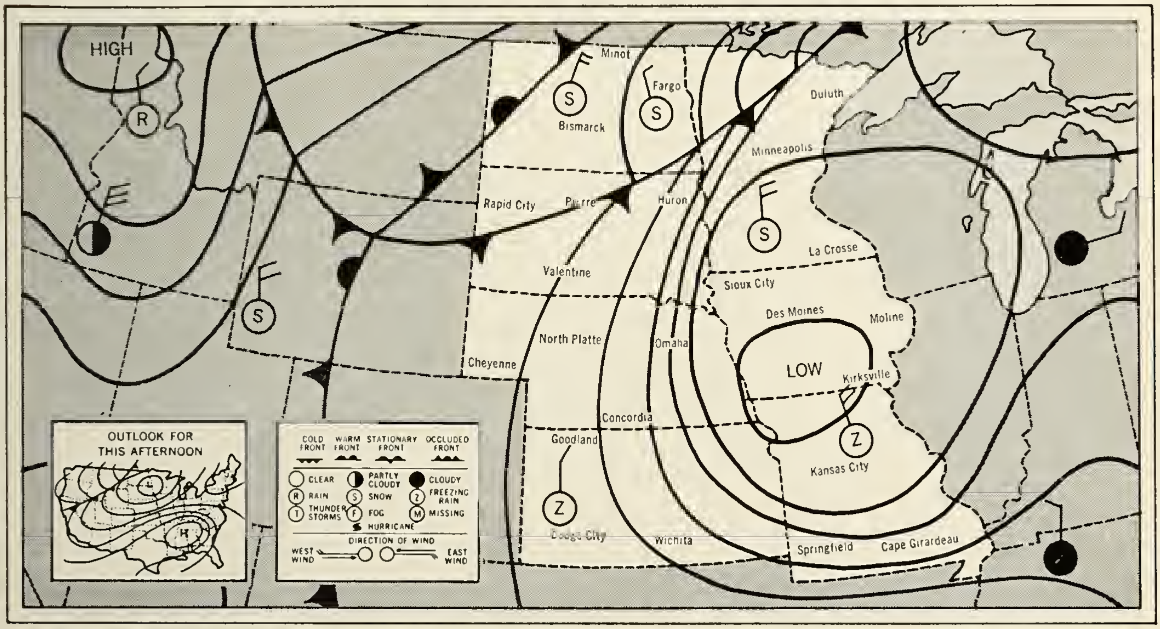

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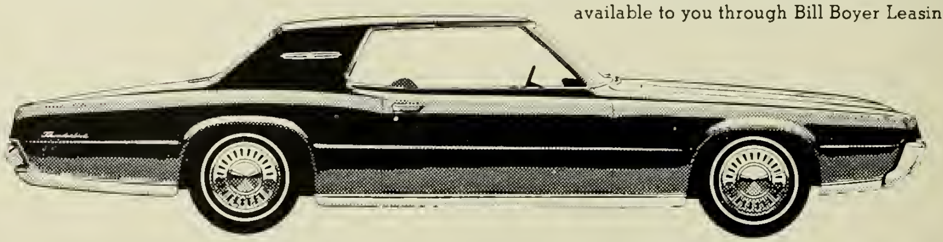

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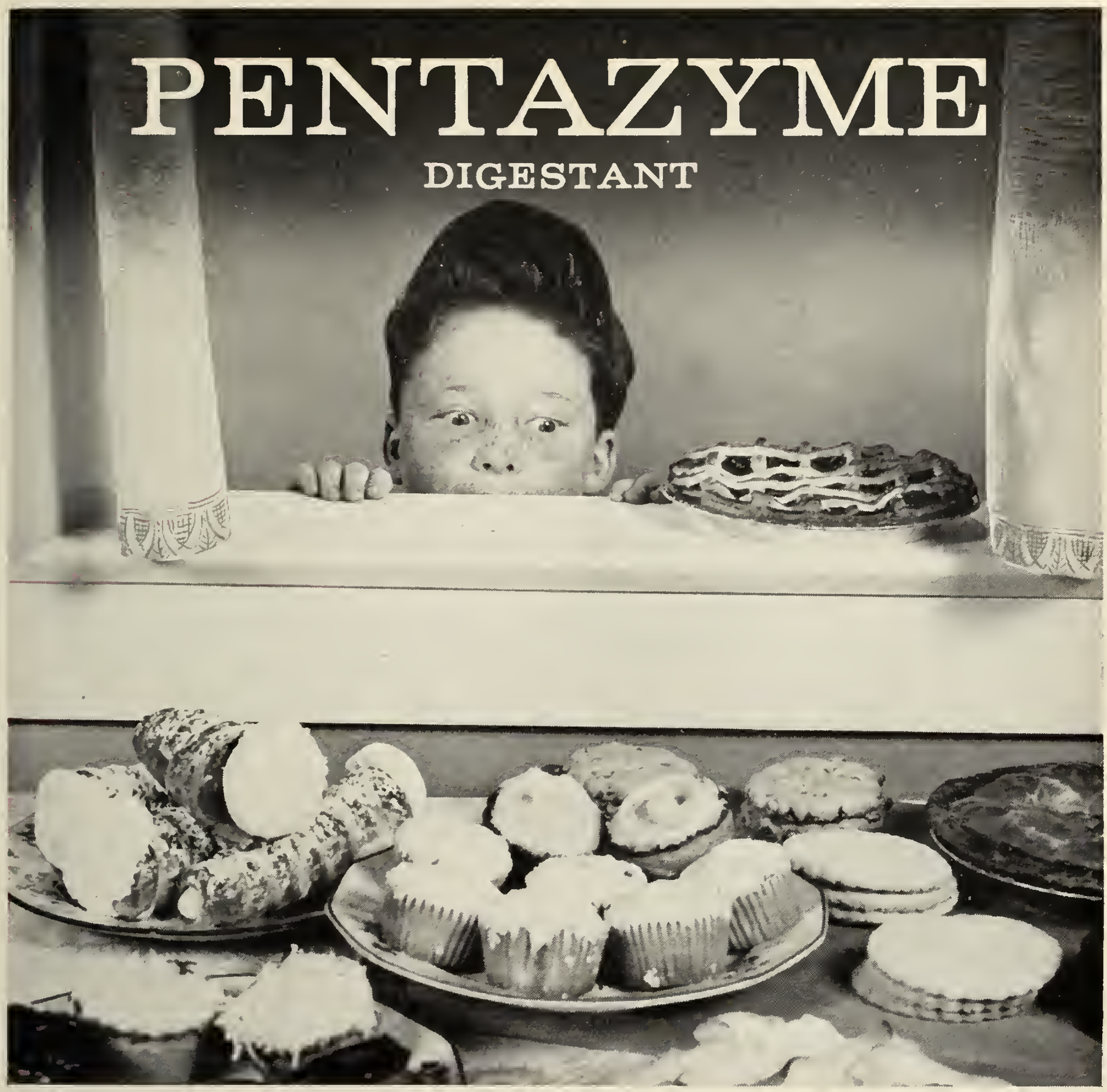

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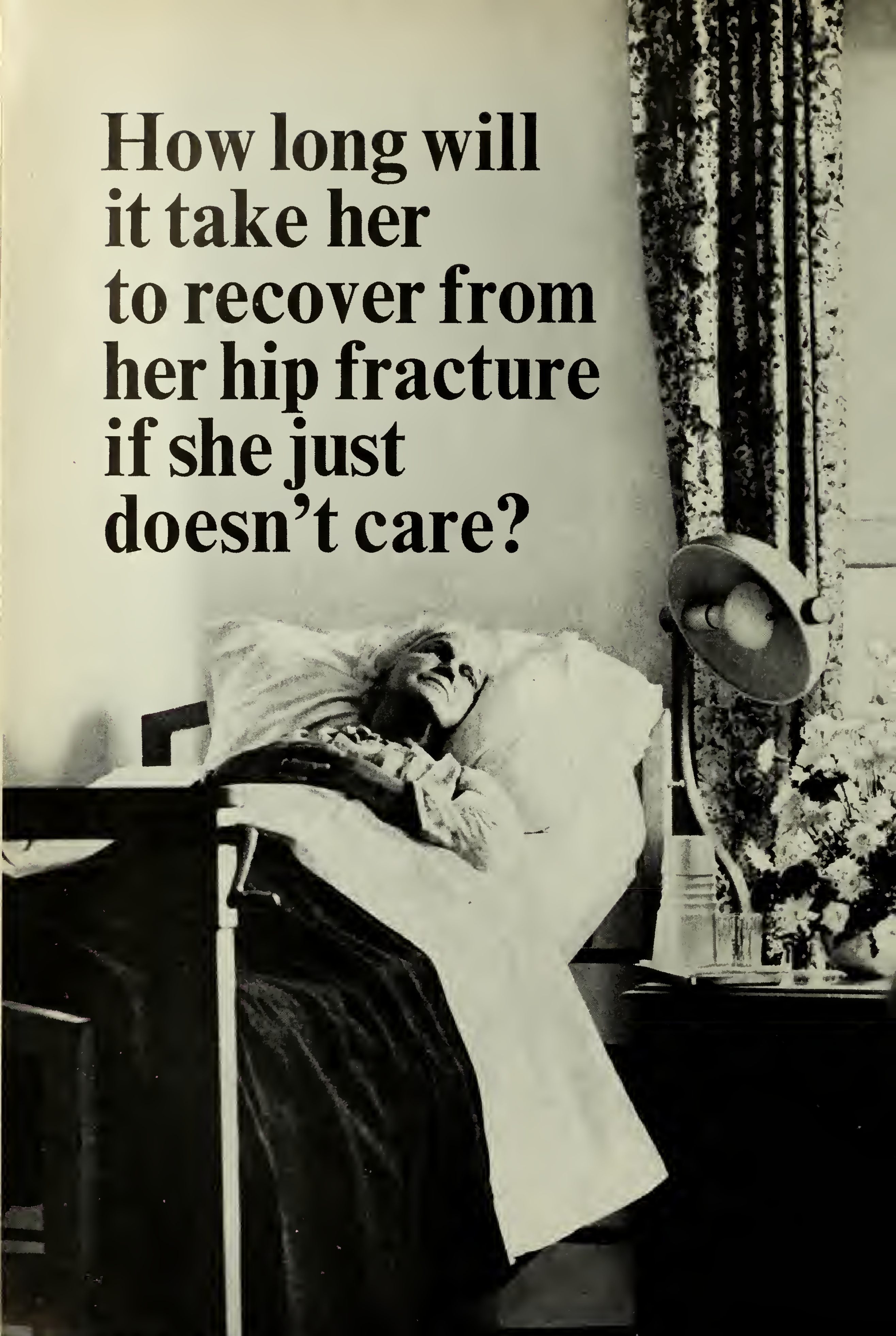

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Dosage: Adults, 1 tablespoonful; children (over 15 years old), 1 to 2 teaspoonfuls; children (4 to 15 years old), 1 teaspoonful. To be taken three times daily 30 minutes before meals.

Contraindications: As with other drugs with CNS stimulating action, Alertonic is contraindicated in hyperactive, agitated or severely anxious patients and in chorea or obsessive compulsive states.

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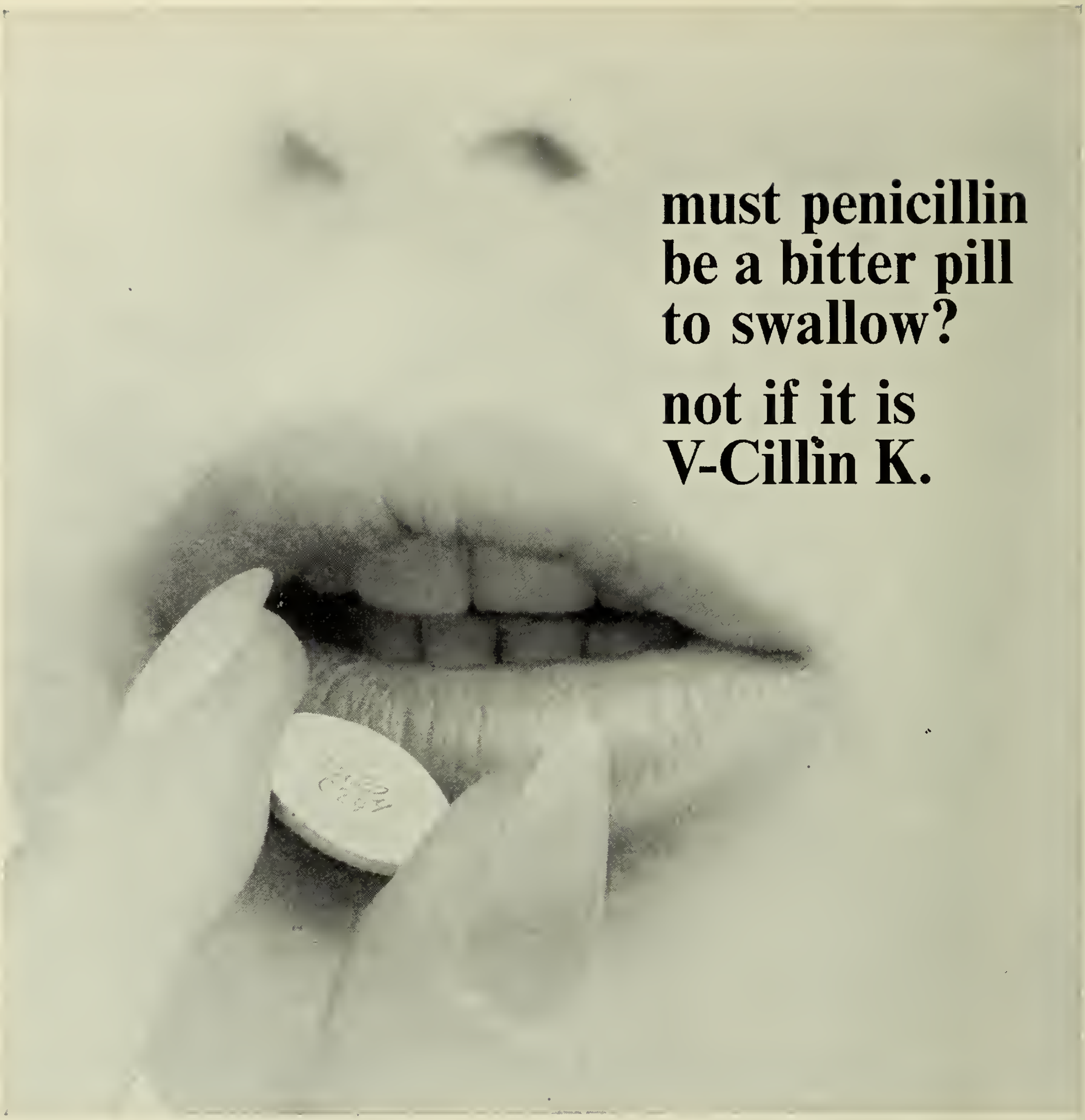
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Gastric Ulcer Associated with Pregnancy

A Case Report and Review of Peptic Ulcers and Pregnancy

CHARLES A. TIETZ, M.D., and WILLIAM N. SPELLACY, M.D.
Minneapolis

PEPTIC ULCERS constitute a common disease, but their frequency of occurrence is different in the two sexes. The incidence of peptic ulcers has been reported at 6% in males and 1.7% in females; the ratio of duodenal to gastric ulcer is 7:1 in both sexes.[1,2] There are many reports in the literature of the occurrence of duodenal ulcers during pregnancy but the association of a gastric ulcer and pregnancy is extremely rare, and we have found no papers dealing with this specific problem. The purpose of this paper is to present the case report of a patient with a gastric ulcer occurring during pregnancy and to review the literature on the problem of peptic ulcers and pregnancy.

CASE REPORT

A 21-year-old unmarried, gravida I, white female, whose expected date of confinement was Dec. 27, 1963, was followed in the University of Minnesota Hospitals prenatal clinic from Oct. 31, 1963. Her past history was complicated because of a nerve deafness occurring at age 3 from an unknown cause.

In November 1962, the patient was seen in the Medical Clinic with a complaint of postprandial epigastric distress and melena. The physical examination at that time showed minimal epigastric tenderness and bilateral eighth nerve deafness. An upper gastrointestinal X-ray showed a lesser curvature gastric ulcer. The patient was treated with bland diet, antispasmodics, mild sedation, and antacids. No gastric ulcer could be demonstrated in a repeat gastric X-ray series in December 1962. The patient was asymptomatic until April 1963, when she returned to the Medical Clinic because of the recurrence of her epigastric pain. Another gastric X-ray again demonstrated the ulcer (Fig. 1). The patient's symptoms became worse, and in May 1963, she complained of nausea, vomiting, and melena. She was hospitalized and was found to be pregnant. Her treatment included bed rest, mild sedation, bland diet of 6 small feedings per day, antispasmodics, and antacids. A hematologic examination showed a blood type O, Rh positive. The patient's hemoglobin was 9.1 gm. percent and the serum iron was 15 μg. percent. The anemia was corrected with intramuscular injections of iron. Stool guaiac tests at first were positive but later became negative. She was discharged after one week of hospitalization. The remainder of her prenatal course was uncomplicated.

The patient was admitted to the hospital in active labor on Dec. 26, 1963. After a total labor of fourteen hours, she delivered a 3,320 gm. normal male infant over a left mediolateral episiotomy, using pudendal block anesthesia. The patient's postpartum course was normal. She had 3 eight-hour overnight gastric collections, which

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CHARLES A. TIETZ, *and* WILLIAM N. SPELLACY *are with the Department of Obstetrics and Gynecology, University of Minnesota Medical School, Minneapolis.*

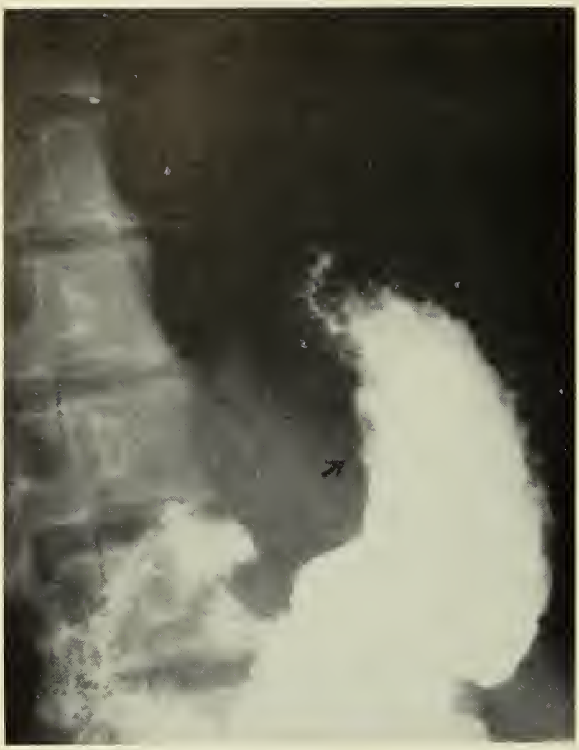

Fig. 1. Upper gastrointestinal X-ray series, taken during pregnancy, demonstrates the greater curvature ulcer at the end of the arrow.

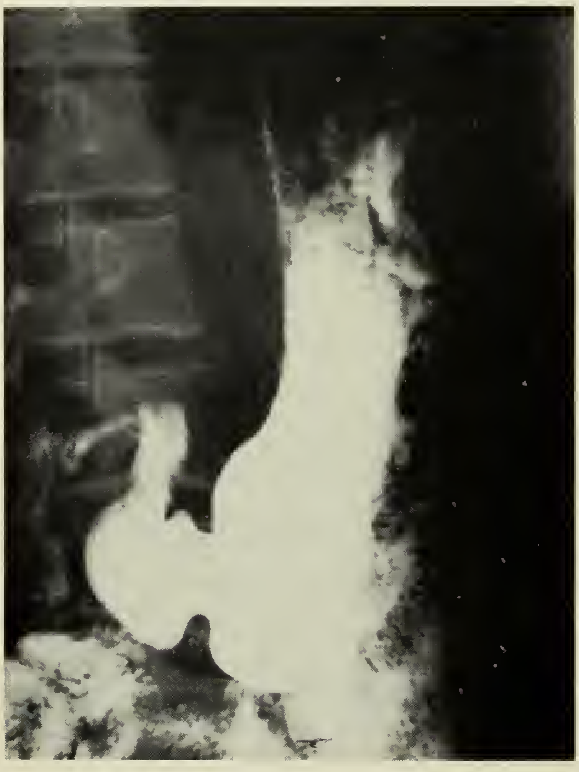

Fig. 2. Upper gastrointestinal X-ray series, taken postpartum, shows the healed ulcer site.

were negative for free acid. A repeat upper gastrointestinal X-ray series again demonstrated the ulcer. A peptone stimulation test produced the normal amount of free acid; a gastroscopic examination showed the ulcer to have a benign appearance; and a gastric washing was negative for tumor cells.

The patient remained on her medical treatment, and, at eight weeks postpartum, a repeat upper gastrointestinal X-ray series failed to reveal the gastric ulcer (Fig. 2). She has remained asymptomatic and presumably has healed her ulcer. A histamine stimulation test and gastric X-ray study were repeated at six months postpartum and were normal.

DISCUSSION

Clinical observations of female patients with known peptic ulcers during pregnancy have led to the conclusion that most of these patients experience improvement or relief of their symptoms. Clark interviewed 400 women in whom peptic ulcer was demonstrated either by an X-ray or at surgery. There had been 344 pregnancies by 118 of these women during the active ulcer state. During 90% of the pregnancies, the ulcer symptoms improved or disappeared. A recurrence of symptoms occurred postpartum, 50% recurring by three months, 75% recurring by six months, and all symptoms recurring by two years postpartum.[3]

There are many studies of the gastric physiological changes occurring during pregnancy. Murray and associates[4] measured the volume of gastric secretion at ten-week intervals during normal pregnancy and postpartum and found that there is a reduced volume of secretion at the thirty-week period. When histamine was given as a stimulus to secretion, there was a depressed response in the first thirty weeks of pregnancy as compared with the last ten weeks of pregnancy and the postpartum period.

The reasons for the clinical improvement in ulcer symptomatology and the findings of a decreased gastric secretion during pregnancy remain unknown. Investigations have studied various hormone effects on the stomach, plasma histamine concentrations, and plasma histaminase levels during pregnancy.

Chorionic gonadotropins, lactogenic hormone, estrogen, progesterone, and the corticosteroids are found in increased concentrations during pregnancy. It is known that the corticosteroids can be ulcerogenic, and one would expect an exacerbation of ulcer problems during pregnancy. The studies of Booth and co-workers[5] have shown that most, if not all, of the glucocorticoid excess in pregnancy is protein-bound and, therefore, inactive. Thus, there is probably little ulcerogenic activity from the corticosteroids.

Progesterone also may be ulcerogenic. Bernstine and Friedman stated that patients with known peptic ulcers, who were given exogenous progesterone during their pregnancy, experienced exacerbations of previously quiescent ulcer symptoms.[6] The experimental data available on the effect of estrogens in gastric physiology are equivocal. Studies have shown that the amount of gastric acid output increases in dogs with lactation.[7,8] McCarthy and associates[8] also gave dogs injections of lactogenic hormone but could not produce any change in the gastric acid output. This is probably enough justification to discourage breast feeding in those patients who have an active ulcer. Gonadotropins probably do not affect peptic ulcers. Sandweiss and co-workers[9,10] surgically produced ulcers in dogs and then treated them with gonadotropic or anterior pituitary-like hormones in a controlled study. They found that there was a regression of the ulcers. This experiment was then extended to include human beings, and, of 18 patients with active peptic ulcer symptomatology who were treated with exogenous gonadotropins, 61% became symptom free. The same results, however, were obtained with placebos. No change was observed in the measurements of acid secretions during the gonadotropin therapy.

It has been shown that the plasma histamine level rises linearly during pregnancy; however, this is not correlated with the acid output or the response to a histamine stimulation test.[11] Other studies have shown that the plasma histaminase levels also are markedly elevated during pregnancy, presumably produced by the placenta.[12,13] It is thought that the histaminase inactivates the histamine, and a resulting decrease in gastric secretions occurs during pregnancy.

The management of pregnant patients with ulcer symptoms is medical. Malignant gastric ulcer occurring during pregnancy has been reported.[14] However, gastric carcinoma is extremely rare in females of the childbearing age group, and, thus, it is recommended that the ulcer symptoms be treated without X-ray studies to protect the fetus from irradiation exposure. If severe hemorrhage, obstruction, or intractable pain occurs, X-ray studies may be required during pregnancy.[15] There are autopsy reports of the findings of gastric ulcers responsible for massive gastrointestinal hemorrhage during pregnancy.[16] The usual surgical indications are valid during pregnancy, and subtotal gastrectomy has been performed during pregnancy without harm to the fetus.[17] Langmade did autopsy studies on patients with toxemia and found an increased association of peptic ulcers and toxemia; thus, the epigastric pain of toxemia in some cases may, in reality, be due to an ulcer.[17]

SUMMARY

During normal pregnancy, gastric physiology changes and peptic ulcer symptoms generally improve. The reasons for the changes are not proved. The case report of a patient with a gastric ulcer associated with pregnancy is presented. Management of peptic ulcers during pregnancy is discussed.

Presented at the Minnesota Obstetrical and Gynecological Society meeting, May 1, 1965, at Duluth, Minnesota.

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Intermittent Type-A Wolff-Parkinson-White Syndrome in a Case of Coarctation of the Aorta

AL ANNAMALAI, M.R.C.P., and
G. ANANTHASUBRAMANIAM, M.D.

Madras, India

The first case of Wolff-Parkinson-White syndrome (WPW) was published by Wilson[1] in 1915. Fifteen years later, Wolff, Parkinson, and White gave a comprehensive description of the syndrome with a review of eleven cases.[2] In 1945, Rosenbaum and associates[3] classified WPW complexes as types A and B on the morphological basis of precordial and esophageal leads. Although the spontaneous occurrence of both types in a single patient is uncommon, such a case has been reported by Matter and Hayes.[4] Earlier reports of this syndrome emphasize that the heart is otherwise normal except for paroxysms of rapid heart action, but the association of organic heart diseases is now being recognized.

The associated diseases could be congenital or acquired. Association with coarctation of the aorta in a 14-week-old baby was reported by Bodlander in 1946.[5] Rheumatic, syphilitic, hypertensive, arteriosclerotic, or thyrotoxic heart disease[5] and pseudoaortic stenosis[6] could be associated with this syndrome. In Bodlander's case, WPW complexes occurred in all complexes in all leads at certain times, yet completely normal complexes were noted at other times. In our case, the WPW complexes were alternating with normal complexes in the same leads. Since this alternating variety has been less frequent, we preferred to report this case.

CASE REPORT

A 23-year-old man was admitted for a checkup on June 2, 1965, nearly two years after an operation for coarctation of the thoracic aorta. Blood pressure was recorded as 160/100 in the arms and 170/120 in the legs. His pulse was 80 per minute and regular. An ejection murmur was heard over the precordium, with no thrill.

An electrocardiogram taken the same day (Fig. 1) showed intermittent WPW complexes, alternating with normal complexes. They were made prominent by overnight sedation and administration of 100 mg. of phenobarbital sodium one-half hour before the recording. Although exercise was ineffective in abolishing the complexes, an injection of 1/120 grain of atropine eliminated the WPW complexes and a normal sinus rhythm appeared. The WPW complexes were evident again immediately after carotid compression (Fig. 2).

A subsequent electrocardiogram taken on the third day (Fig. 3) showed normal sinus rhythm and disappearance of the WPW complexes.

Routine investigations were within normal limits. Blood cholesterol was 250 mg. percent, blood sugar was 83 mg. percent, blood urea was 40 mg. percent, and serology was negative for syphilis. Urinalysis showed absence of albumin and sugar. Roentgenographic examination revealed left ventricular hypertrophy. Funduscopic examination resulted in Waegner and Keith's Grade I.

DISCUSSION

The essential diagnostic feature of the WPW syndrome is a distinctive electrocardiogram in which the following variations are seen:[7] [1] the P-R interval is shortened, measuring 0.10 second or less, [2] QRS complexes are widened from 0.11 to 0.14 second and slurred, [3] T waves are usually running opposite in direction to QRS, and [4] the P-J interval is normal. During an attack of paroxysmal rapid heart action, these features usually disappear but may persist.

In 1952, Lown and associates[8] reported the "syndrome of short P-R interval, normal QRS, and paroxysmal rapid heart action" in a study of 200 cases. Although it was not their intention to describe this as a variant of the original WPW syndrome, Grant and associates[9] elected to

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AL ANNAMALAI *is additional professor of medicine, and* G. ANANTHASUBRAMANIAM *is assistant professor of medicine, Madras Medical College, Madras.*

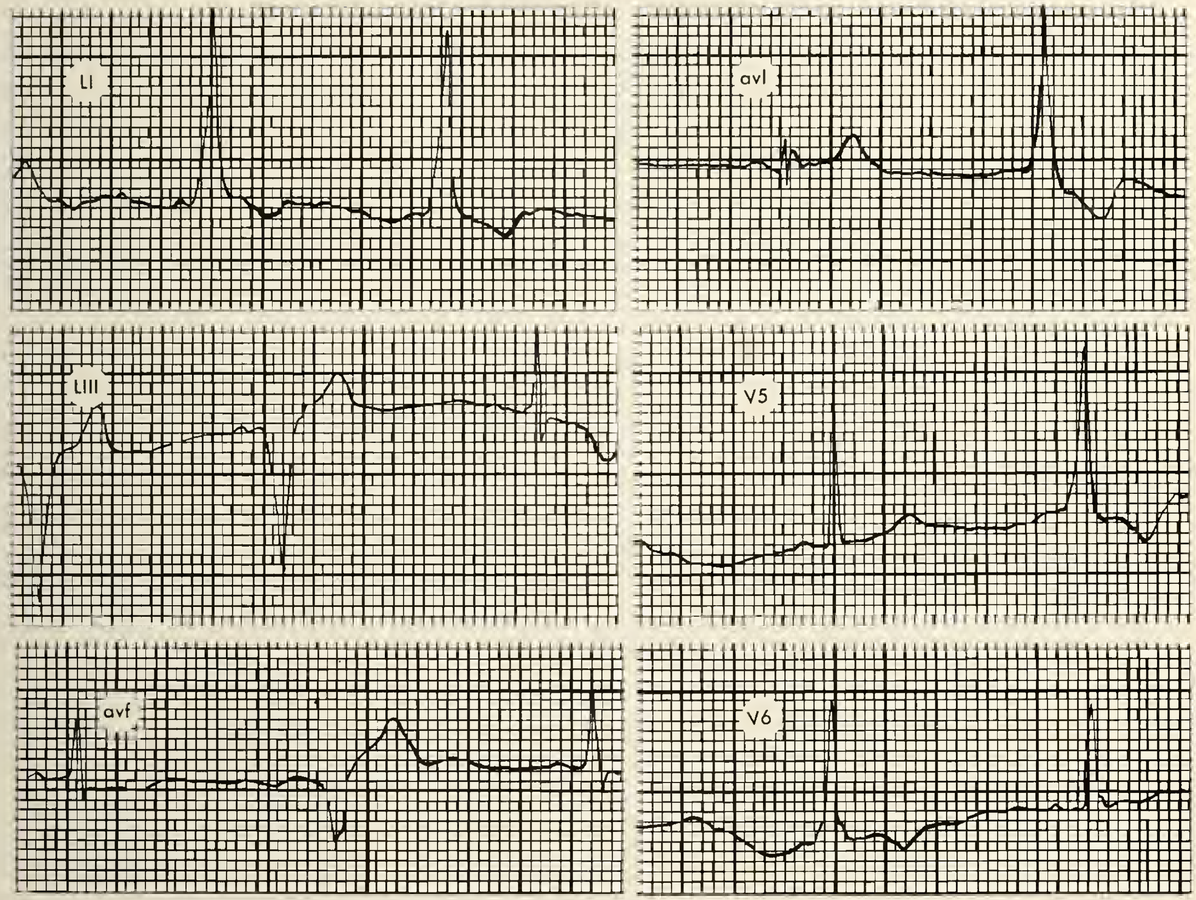
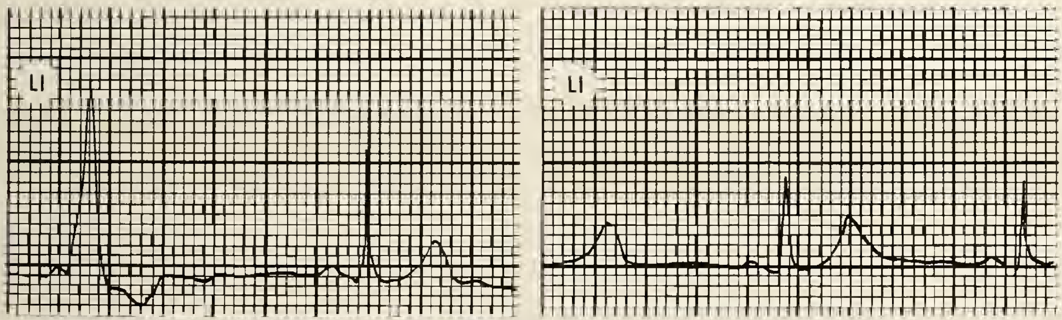
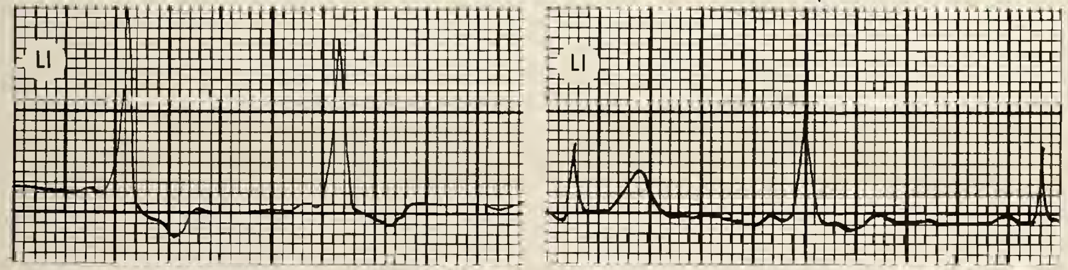


Fig. 1. Electrocardiogram taken on day of admission. Intermittent WPW complexes, alternating with normal complexes



30' after sedation

After atropine I.V.



After exercise

Caro. comp

Fig. 2. Electrocardiogram showing WPW complexes after carotid compression

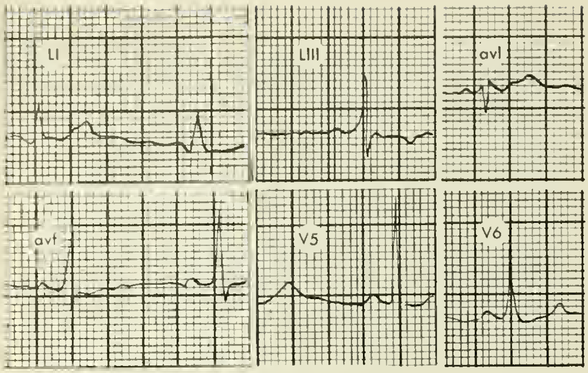


Fig. 3. Normal sinus rhythm and disappearance of the WPW complexes on the third day

refer to the original description as a preexcitation type and the other as the Lown-Ganong-Levine type of WPW syndrome, since both have many similar features. In addition, we have Rosenbaum's types A and B based on the configuration of QRS in precordial leads. In type A, the delta wave and the remainder of the QRS complex are primarily positive in both right and left precordial leads. In type B, the delta wave and the remaining portion of the QRS complex are positive in left precordial leads but negative in right precordial leads. Although this is purely an artificial division, the different configurations may be related intimately to the area of initial ventricular excitation. Our patient may be classified as type A.

The syndrome occurs at all ages and in both sexes but is more frequently in males under 30 years. These patients are apparently healthy subjects who are prone to attacks of supraventricular and ventricular tachycardias. The increasing tendency to recognize associated heart disease has already been mentioned. Even in the absence of organic heart disease, sudden death can occur during an attack of tachycardia.

The characteristic electrocardiographic features are usually apparent in predominantly monophasic leads. Generally, all the complexes in the leads are of the WPW type. In the same individual, a completely normal electrocardiogram could be recorded at times. But WPW complexes also can alternate with normal complexes in the same lead, as in our case, and we feel this is relatively less frequent. The WPW complexes may disappear spontaneously or after exercise or administration of atropine. But reports regarding the effect of drugs and exercise are conflicting. In our case, the WPW complexes were not abolished by exercise nor altered by phases of respiration or intravenous digoxin. Rather, they were eliminated by intravenous administration of 0.6 mg. of atropine and were produced by carotid compression.

We have been successful in bringing out the WPW complexes on 4 occasions after the patient has had overnight rest and 100 mg. of phenobarbital sodium, intramuscularly, half an hour before recording the electrocardiogram. The heart rate slowed down, probably due to rest and sedation. When it was 60 per minute or below, the WPW complexes were brought out. Thus far, our patient has not shown any tendency for paroxysmal rapid heart action, and this may be due to the intermittent nature of the syndrome. It is interesting to see whether this alternating variety progresses to permanent WPW complexes without intervening normal complexes and, if so, whether he is liable to have attacks of tachycardia—just like auricular fibrillation, which could be paroxysmal before it establishes itself permanently. (In an electrocardiogram made after submission of this article, all complexes in all leads were of the WPW type.)

ETIOLOGY

With respect to our case, the etiology is a matter of conjecture. The WPW complexes were not noticed in 1962 at the time of operation. But we are not able to say that they were absent before surgery because of the intermittent occurrence. Transient appearance of it during cardiac catheterization and in myocardial infarction involving the nodal tissue indicates that injury to this region can produce this syndrome. In our case, the normal complexes in lead III and aVf showed persistent S-T depression and T wave inversion which may indicate ischemia of the inferior wall. Since the patient had a congenital heart disease, it is also tempting to postulate the probability of accessory conduction pathways. Also, in view of long-standing hypertension with associated left ventricular hypertrophy and the nonspecific systolic murmur over the precordium, it is possible that this patient may have acquired pseudoaortic stenosis—a condition which is associated with WPW syndrome in nearly 50% of all cases.[6]

The following classification includes all types described and the probable mode of progress of the different types. The numbering of 1 to 5 represents the order of progress.

I. Lown-Ganong-Levine type, with short P-R, normal QRS, and paroxysm of rapid heart action[9]

II. Preexcitation type
  Paroxysmal
    1. Alternating with normal complexes

(Continued on page 494)

Functional Dyspnea

DAVID E. DINES, M.D.

Rochester, Minnesota

Dyspnea is a common problem faced by the practicing physician. Both therapy and prognosis depend on accurate diagnosis. Though the subjective sensation of breathlessness may be a symptom of various conditions, the diagnosis frequently can be narrowed to deciding whether it is cardiac, pulmonary, or functional. It is not within the scope of this paper to go into the practical differentiation of cardiac and pulmonary dyspnea; many good articles have been written on this subject.[1–6]

The physician may be responsible for giving an opinion on the relation of dyspnea to occupation or to disability and the amount and duration of disability and whether there is permanent impairment.

It is important that a complete work-up to exclude the organic causes of dyspnea be carried out, including history and physical examination, X-ray examination of the chest, electrocardiographic examination, and evaluation of pulmonary function.

Functional dyspnea may present in various patterns. It may imply an inability to continue with exercise because of fatigue, muscle aching, chest wall discomfort, or generalized weariness. It can imply shortness of breath from the sensation of choking or tightening in the throat, as in globus hystericus. Commonly, patients complain of the inability to take a deep enough breath. Breathing may be rapid and shallow and lead to chronic hyperventilation. It may be seen with forced bronchospasm, superficially simulating asthmatic wheezing. Just as there are patients with palpitation from preoccupation with the heart, there are patients who have anxiety states manifested by an increased perception of breathing effort.

On physical examination, there has been one important test that I have found useful in distinguishing functional dyspnea: Merely ask the patient to hold his breath and time the breath-holding. I have yet to find a person with functional dyspnea who has been able to hold his breath longer than fifteen seconds. Patients with severe obstructive disease of the airway and marked obstructive ventilatory impairment, as well as cardiac patients, can hold their breath thirty to sixty seconds.

Tests of pulmonary function are of definite value, since the mechanical factors in breathing are not significantly altered in functional dyspnea. The lung volumes are normal, the distribution of inspired gas is normal, and the arterial oxygen saturation is normal at rest and with exercise. The ventilation (tidal volume, respiratory rate, and minute volume [liters per minute]) may be abnormal if the patient is hyperventi-

RESULTS OF PULMONARY FUNCTION TESTS

	Estimated normal	*Observed value*
Pulmonary volumes		
Vital capacity: expiratory, liters	5.7	5.84
Inspiratory, liters	5.7	
Residual volume (RV), liters	1.9	2.19
Total capacity (TC), liters	7.6	8.03
RV/TC × 100 (%)	≦30	27
Functional residual capacity, liters	3.4	4.57
Expiratory reserve, liters	1.5	2.38
Maximal breathing capacity, liters per minute	155	99
Maximal midexpiratory flow, liters per second	≧2.5	3.3
Expiratory slowing	0	0
Nitrogen-washout index, percent N_2	2.5 or less	0.4
Arterial oxygen saturation (oximeter) (%)		
Resting (air)	95-98	99
Resting (oxygen)	100	100
Before exercise (air)	95-98	99
Exercise (air) for 5 minutes	no fall	99
Exercise (oxygen)	100	
Ventilation (at sitting rest, breathing oxygen)		
Liters per minute		11.74
Respirations per minute		20.2
Average tidal volume, ml.		581

DAVID E. DINES *is with the Section of Medicine, Mayo Clinic and Mayo Foundation, Rochester.*

lating. The mechanics of breathing (maximal breathing capacity and maximal midexpiratory flow rate) are normal. However, the maximal breathing capacity may be very low, signifying that the patient has not made a maximal effort. This is helpful when it is present and fits the overall picture.

CASE REPORT

A 17-year-old male student was seen on June 1, 1965, because of dyspnea of twelve months' duration, associated with chest pain and chronic fatigue. He had had symptoms since June 1964, when he was exposed to camphene spray (Toxophene®).

Physical and neurologic findings were normal except that the patient was unable to hold his breath longer than twelve seconds. The usual laboratory tests, X-ray examination of the chest, and electrocardiographic examination did not show any abnormality. Examination of the ears, nose, and throat showed a hypoactive left labyrinth.

Pulmonary function was normal except that maximal breathing capacity was decreased to 99 liters per minute (see table). The respiratory rate was increased to 20.2 liters per minute. Minute volume was very large—11.74 liters per minute, normal, 6 liters per minute.

COMMENT

This patient presented with functional dyspnea and chronic fatigue. The inability to hold his breath, when other physical findings were negative, confirmed the diagnosis. Pulmonary function was normal except for maximal breathing capacity, which was depressed and signified a poor effort. Confronted with the findings, the mother admitted that her son had been nervous, depressed, and withdrawn over the past year. His father had been dead for three years.

SUMMARY

Dyspnea is a common problem in diagnosis. Patients with functional dyspnea can present with several patterns, and both therapy and prognosis depend on an accurate diagnosis. The breath-holding test has been of value on physical examination and requires only a few minutes. Tests of pulmonary function are important, particularly when there is evidence of hyperventilation and of poor effort in maximal voluntary ventilation. The diagnosis should not be made without a complete work-up, including studies of pulmonary function during rest and during exercise.

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Intermittent Type-A Wolf-Parkinson-White Syndrome in a Case of Coarctation of the Aorta—(Continued from page 492)

Al Annamalai, M.R.C.P., and G. Ananthasubramaniam, M.D.

2. Irregular, occurring at random in one or more leads
3. Intermittent, all either normal or WPW complexes[5]

Persistent

4. Except during tachycardia
5. Even during tachycardia[7]

SUMMARY

We have reported a case of intermittent type A, Wolff-Parkinson-White syndrome in a patient with coarctation of the aorta. Attention is drawn to its association with organic heart diseases. Overnight rest and intramuscular administration of 100 mg. of phenobarbital sodium one-half hour before recording the electrocardiogram are suggested to produce the complex in the intermittent variety. Various types are mentioned and a classification is suggested.

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The Weak Patient

GEORGE C. FLORA, M.D., and A. B. BAKER, M.D.
Minneapolis

WEAKNESS IS ONE OF THE more common problems encountered in the practice of medicine. True weakness is due to involvement of the lower motor neuron. This cell has its body in the cranial nerve nuclei or the anterior horn cell column of the spinal cord and its axon passes through motor nerves, cranial or peripheral, to innervate specific muscle fibers. Involvement of this system is characterized by true weakness of the innervated musculature, associated with atrophy, hyporeflexia, and hypotonia, and if the cell body itself is involved by fasciculation of muscle bundles as well.

Probably the most useful aid to the physician in diagnosing a given case of lower motor neuron involvement is an exact knowledge of the onset of the disease. A knowledge of the onset of a disease and a familiarity with the causes common to the specific age group will permit good diagnostic handling of these cases.

ACUTE ONSET IN INFANCY AND CHILDHOOD

Poliomyelitis. Infantile paralysis has classically been the prototype of lower motor neuron deficit which occurs acutely in childhood. Since the advent of successful vaccination, its frequency has decreased but it is not likely to entirely disappear. The clinical picture in childhood is usually that of a diphasic systemic infection most frequently of an upper respiratory type. The septic picture is that of 2 bouts of low grade fever; the second episode is associated with severe malaise which may be followed by the development of lower motor neurone weakness. The motor deficit may be progressive for a period of hours or for a maximum of twelve days. This disease classically and specifically involves the motor cells of the cervical and lumbar cord and may also localize to the medulla. The resultant paralysis is manifest in one or more of the extremities or in the dysfunction of the bulbar musculature producing impaired breathing, speaking, or swallowing.

The clinical picture before the development of lower motor neuron deficit, which alerts the physician to the probable diagnosis, is the evident severity of the systemic illness which appears out of proportion to both the height of the fever and evident foci of infection. During this period of acute illness, the patient manifests marked tenderness of his muscles both to stretch and pressure. This is most commonly localized to the muscles of the neck, back, and thighs. The patient shows increased nuchal tone, "tripod positioning" when attempting to sit, and positive Brudzinski's and Kernig's signs. As weakness develops, it will usually be found to involve but a few muscles of a single extremity. There is an associated hyporeflexia.

The prognosis with good treatment has reduced the mortality rate to less than 2% of recognizable and diagnosed cases. Severe crippling occurs in 20% of the cases of the acute poliomyelitis which are diagnosed.

The treatment of acute poliomyelitis is subdivided into 4 major goals. The first is the prevention of death, the second is relief of pain, the third is the provision of adequate rest, and the fourth is the prevention of deformities. To prevent death in acute polio, one must counteract the respiratory insufficiency which threatens mortality in a certain number of cases. This is done by maintaining an airway with tracheotomy, adequate suctioning and postural drainage, and by supporting compromised respiratory muscles with mechanical respirators when the need arises. The relief of pain is best provided by heat and salicylates and with strict avoidance of narcotics and strong sedation. Adequate rest is assured if the respiratory impairment is supported and pain adequately controlled. The pre-

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GEORGE C. FLORA *is with the Division of Neurology, University Hospital, Minneapolis, and* A. B. BAKER *is professor and director, Division of Neurology, University of Minnesota Medical School, Minneapolis.*

vention of deformities in the paralyzed extremities is accomplished by use of gentle range of motion, proper positioning with posterior splints, sheet supports, and support of the body with bed boards.

Guillain-Barré syndrome. In the younger age group this syndrome presents as a lower motor neuron weakness most prominent in proximal muscles and is bilaterally symmetrical. It is associated with radicular pain and acute muscle tenderness. The disease is also characterized by "stocking" type hypalgesia or an ascending segmental level of hypesthesia and hypalgesia. Guillain-Barré is not associated with systemic signs or a febrile response.

On examination the weakness is severe and classically associated with bilateral facial palsy. Diagnosis can occasionally be further established by the absence of cells in the cerebrospinal fluid in the presence of an elevated cerebrospinal fluid protein in the range of 80 to 100 mg. percent.

Treatment consists of symptomatic care. If bulbar function is impaired, support of the respiratory function with tracheotomy and respirators may become necessary. During the period of severe motor weakness, passive range of motion and proper positioning for the prevention of deformities is paramount.

PROGRESSIVE COURSE

Infantile muscular atrophy (Werdnig-Hoffmann). This sporadic condition does not become apparent until the sixth to ninth month of life in a child who has developed quite normally, at which time a symmetrical weakness of the trunk and limbs slowly develops. Widespread atrophy develops with loss of all motor reflexes. The condition spreads to involve the intercostal and bulbar musculature which results in respiratory decompensation causing death within six to twelve months. There is no therapy for this disorder.

Progressive muscular dystrophy (infantile type of Duchenne). This condition, though not primarily neurogenic in type, is included because of its frequency and primary manifestation of weakness. It is a primary muscle disease of unknown etiology which is transmitted as a sex-linked recessive. It affects chiefly males between the ages of 1 and 4 years. The clinical picture is that of a progressive weakness of the pelvic and lower extremity musculature. Often there is a pseudohypertrophy of the muscles of the calves. The child first manifests weakness when attempting to climb stairs or to rise from the prone position. Rising from a lying position is accomplished by the classical maneuver of "climbing his own legs." As the weakness of the lower extremities and pelvis progresses, the gait becomes waddling with marked protrusion of the abdomen and a severe lordosis. The prognosis for this condition is poor and death usually occurs before the twentieth year. There is no therapy for this condition.

ACUTE ONSET IN THE ADULT

Poliomyelitis. This has been the most common cause of lower motor neurone deficit in this age group; hopefully it has decreased permanently since the advent of protective vaccines. The diagnosis has been discussed in the previous section.

Guillain-Barré syndrome. This is presently the most common cause of acute lower motor neuron deficit in this age group. The diagnosis and treatment have been discussed in the previous section. The prognosis for total recovery is favorable. Most cases are self-limiting in three weeks and will then show improvement. Recovery may occasionally be delayed as long as one year in severely involved cases. If bulbar involvement occurs, the prognosis is less favorable and the mortality rate rises to 30%.

Familial periodic paralysis. This condition is heredofamilial, although sporadic cases do occur due to an inborn error of potassium metabolism. The condition chiefly affects males and is characterized by recurrent sudden onset, at night or during the early morning when awakening, of severe motor weakness. The weakness classically begins in the lower extremities and ascends, with the total duration of paralysis lasting from six to ten hours. During the weakness there is an absence of reflexes, a loss of motor tone, a bradycardia, and at times, a partial heart block.

Treatment of this condition is directed towards prevention of the attacks. The factors which tend to precipitate paralytic attacks are glucose, high carbohydrate meals, insulin, alcohol, and adrenocortical hormones. Consequently, the treatment is that of low carbohydrate intake, with less than 100 gm. per meal permitted and with very light meals before sleeping. Total abstinence from alcohol is absolutely mandatory. Potassium chloride, 2 to 10 gm. per day, is administered to help counteract the chemical abnormality which shifts extracellular potassium into cells to precipitate the acute episode of weakness.

Hypopotassemia. Profound lower motor neuron weakness can develop when the body's stores of potassium are depleted. Depletion of potassium can occur with prolonged diarrheas and severe vomiting and in hepatic cirrhosis, diabetic acidosis treated with insulin, long-term adrenocorticotropic hormone or cortisone therapy, and chronic renal disease.

The symptom complex is that of anorexia, nausea, abdominal distention, delirium, and cardiac abnormality with profound motor weakness.

The diagnosis, if not clear from the clinical picture, can be verified by electrocardiogram which classically shows a depression of the S-T segment and an inversion of the T wave.

The treatment consists of administration intravenously of 40 to 80 mEq. of potassium in 5% glucose. This therapy is repeated to counteract recurrence until the underlying deficit can be corrected. The electrocardiogram (EKG) permits laboratory titration of this therapy.

Hyperpotassemia. Profound lower motor neuron dysfunction can occur in the presence of increased circulating serum potassium. The body stores of potassium may be elevated when renal failure is present, when oliguria occurs, or when the administration of parenteral potassium is greater than that which the body can normally excrete, seen especially in postsurgical cases. The increased potassium can be confirmed by electrocardiogram, which shows prolonged QRS interval with a high peaked T wave.

The treatment for this condition is the administration, intravenously, of 10 to 25% hypertonic saline in glucose. This may be repeated until the EKG returns to normal level.

Lymphoblastoma of the spinal cord. The acute onset of focal motor weakness in the limbs within this age group suggests metastatic disease. The lesion produces pyramidal signs below it, manifested by a diplegia or quadriplegia and a sensory "level" with loss of pain or touch appreciation below the site of the lesion. Diagnosis can be established by X-ray evidence of mass lesion within the chest or the abdomen, blood studies, or biopsy for evidence of leukemic or Hodgkin's abnormality. Therapy, although palliative, can be of significant benefit, especially easy decompression and deep X-ray therapy to the site of the lesion and treatment of the systemic disease.

GRADUAL ONSET

Amyotrophic lateral sclerosis. This condition is characterized by the insidious onset of weakness, muscle atrophy, and fasciculations. The focal atrophy usually develops symmetrically in the small muscles of the hands or tongue and may spread to involve all the muscles of the body. The condition finally ascends and involves the lower motor neurons of the medulla resulting in a severe dysphagia and dysarthria. Concurrent with the developing weakness there is a pyramidal deficit, usually evident in the lower extremities as positive toe signs and hyperactive deep reflexes, both apparent in spite of the associated lower motor neuron deficit. The course of the disease is rapidly progressive. Death usually occurs within two years of the time the patient first consults his physician for this condition. The death is one of bulbar decompensation with aspiration or cardiorespiratory arrest.

Treatment is symptomatic, with no specific remedy yet discovered. Dimercaprol (BAL) and corticoids have been utilized.

Progressive muscular atrophy (Aran-Duchenne). This condition is characterized by a slowly progressive lower motor neuron deficit which develops in the small muscles of the hands symmetrically and spreads to involve the forearm, arm, and finally the shoulder girdle musculature. Simultaneously, or following the onset in the upper extremities, the lower extremities may also become involved with atrophy of the small muscles of the feet, which spreads to involve the more proximal muscles. The condition may finally progress to involve the intercostal and bulbar musculature. The disease is characterized by profound weakness, loss of deep tendon reflexes, atrophy, and fasciculations of the involved muscles, but with no sensory or pyramidal deficits. Therapy for this condition is symptomatic.

Progressive muscular dystrophy (Landouzy-Dejerine). This condition is a heredofamilial disorder of the muscles which is transmitted as a dominant. The onset occurs in either sex at 14 to 17 years of age with the primary involvement occurring in the shoulder musculature and face. The disease produces a classically dystrophic face, which is "hatchet-like" with a "transverse" or myopathic smile. The face is mask-like, with little expressiveness. The upper extremity deficit produces winging of the scapulae which may appear above the shoulder level. As the disease progresses, the patient's lower extremities and pelvic girdle may become involved, impairing gait and producing a lordotic stance. The course of this disorder is one of slow progression which disables only after many years. With the loss of muscle strength, severe contractures develop necessitating wheelchair existence. The disorder does not greatly shorten the life expectancy of the involved patient. Treatment is symptomatic.

Neuritic muscular atrophy (Charcot-Marie-Tooth). This condition is a familial disease which affects several siblings of a given family. The condition is one of slowly progressive weakness and atrophy involving the feet and legs of a young adult. The foot shows profound weakness with foot drop or club foot developing. The legs then become weak and atrophied with preservation of normal-sized thighs which gives the individual a "stork-legged" appearance. The condition frequently has associated sensory impairment of the peripheral nerve type with "stocking" hypesthesia and hypalgesia. The condition rarely involves the upper extremities. The progress of the disease may halt at any time with rather permanent plateauing. Progression with fatility is not known. If independent ambulation is jeopardized suitable aids may be prescribed.

Myotonia dystrophica. This condition is a strongly hereditary disorder of multiple body systems which commences between the ages of 20 and 30 years of age in either sex. Early in the course of the disease the patient manifests myotonia, a relaxation difficulty following forceful contraction of the muscles of the hand. Neurological examination reveals myotonia when shaking hands with the patient; the grip relaxes slowly over several seconds. Associated with myotonia there is an atrophy of the facial and temporal muscles which classically also involves both sternocleidomastoids. The "myotonic face" develops showing frontal alopecia, absent sternocleidomastoids and "hawk-like" features. Premature cataracts occur and testicular atrophy or ovarian dysfunction is present. The patients who have this involvement characteristically show some degree of personality alteration with loss of instinctual drive as well as mental acuity. Once the classical syndrome develops, it is not transmitted due to the endocrinal abnormalities. Previous generations may have had partial deficits. Treatment is palliative. The myotonia may be beneficially treated with quinine. Prognosis for life is good.

Polymyositis (dermatomyositis). This condition is not neurogenic; however, the progressive muscular atrophy associated with weakness which is seen in this condition mimics lower motor neuron disease. This condition is characterized by pain and tenderness of the muscles which is associated with an elevated sedimentation rate and an abnormal activation pattern on electromyographic recordings. Atrophy and hyporeflexia may develop, but these are seen relatively late in the course of the disease and are believed to be myopathic rather than neurogenic. The diagnosis may be established by muscle biopsy which shows an inflammatory reaction. Treatment is that of collagen disease, with corticoids presently the mainstay of the regimen.

Myopathy with metabolic diseases: myxedema. This condition may produce weakness of the lower extremities with little evident atrophy. Sensory deficit of the peripheral nerve type can occur. The syndrome may be established by associated findings such as nonpitting edema of the lower extremities, coarse skin, enlarged tongue, low blood pressure, lassitude, loss of the lateral eyebrow, and positive laboratory findings. Treatment is specific and consists of the administration of therapeutic dosages of thyroid.

Thyrotoxic myopathy. This condition is seen chiefly in males and involves the muscles of the pelvic and shoulder girdles. The deep tendon reflexes remain normal or hyperactive, but muscle wasting may occur. The symptom complex may be diagnosed by the associated findings of weight loss, increased fatigability, restlessness, exaggerated physiological tremor, exopthalmus, and increased basal metabolic rate. Laboratory confirmation is now available with radioactive iodine studies. Treatment is directed towards surgically or medicinally counteracting the basic endocrinal abnormality.

Addison's disease. This condition is characterized by generalized muscle weakness without evidence of atrophy or fasciculation. The reflexes may be decreased. The associated symptomatology includes increased fatigability, pigmentary changes of the exposed skin, anorexia, hypotension, and resultant syncope. This condition is treatable by replacement therapy of the adrenocortical hormones by implantation.

ACUTE ONSET IN OLD AGE

Guillain-Barré syndrome. This condition is the most common cause of acute lower motor neuron deficit in this age group. The diagnosis and treatment have been discussed in the previous section. Prognosis is not as good as in earlier periods of life. Permanent residuals are more commonly encountered after the age of 60 years.

Disturbances of serum potassium. These are frequently encountered in patients who are prone to primary systemic diseases which predispose to these disturbances. The diagnosis and treatment of these disorders have been discussed in detail in previous sections.

Hematomyelia. This disorder, which is occasionally encountered, is usually precipitated by severe exertion of a lifting type. The clinical picture is that of acute radicular pain. The extent of the neurological deficit is determined by the extent of parenchymal damage. The course of hematomyelia is classically that of vascular disease, reaching a rapid maximum deficit and then remaining stationary or showing improvement.

Metastatic carcinoma to the spine. Acute lower motor neuron deficit of a focal type, associated with radicular discomfort, must make one seri-

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Primary and Secondary Blastomycosis of the Lungs and Skin

DAVID T. SMITH, M.D.

Durham, North Carolina

THE FUNGUS infections simulate tuberculosis more closely than they do acute or chronic bacterial infections. Apparently, neither exotoxins or endotoxins are produced by fungi, but the delayed tuberculin-like allergy is usually present and the tissue reactions are of the granulomatous type.

Histoplasmosis duplicates nearly all of the characteristics of tuberculosis, except it is not infectious directly from patient to patient. The primary infection is usually followed by localized areas of calcification, dissemination is to the same organ system, and a reinfection-type lesion occurs predominantly in the upper lobes.

Coccidioidomycosis can also produce localized calcified lesions but does so less frequently than tuberculosis. The dissemination occurs in the same manner as in tuberculosis. A localized area of infection in a bone or in some organ from the primary dissemination may reactivate after a period of years, but there is no true reinfectious type of pulmonary disease in the upper lobes.

Blastomycosis shows a primary type of infection in the lungs and in the skin, which may or may not be followed by dissemination, but no reinfection of the upper lobes of the lungs has been observed. Enlargement of the regional lymph nodes, which is so characteristic of tuberculosis, histoplasmosis, and coccidioidomycosis, occurs only rarely with blastomycosis. Localized areas of calcification following the primary infection have never been seen. Perhaps, the reduction in lymphadenopathy and the absence of localized areas of calcification depend upon the absence of caseation in the primary lesions. The absence of caseation may, in turn, depend upon the mild degrees of tuberculin-type allergy which develops in patients with blastomycosis.

The delayed-type allergy to blastomycosis is slow in developing. We have found the skin test negative in 30 to 50% of patients at the time the diagnosis was made by culture or biopsy. In most, but not all instances, the skin test became positive in the next two to four months. The degree of the allergy, when present, is much less than that seen in tuberculosis, histoplasmosis, and coccidioidomycosis. Skin reactions to blastomycosis may last only twenty-four hours and, therefore, be read as negative if not inspected at the twenty-four-hour period.

PRIMARY PULMONARY BLASTOMYCOSIS

The primary pulmonary lesions of blastomycosis are usually solid pneumonic areas which may be confused with lobar and lobular pneumonia or tuberculosis. Isolated solid lesions located near the hilum are frequently mistaken for primary carcinoma of the lung and resected.

Enlargement of the hilar lymph nodes is unusual in blastomycosis in contrast to tuberculosis, histoplasmosis, and coccidioidomycosis. We found only one in over 100 cases of blastomycosis, whereas Abernathy has seen 4 in 70 cases of pulmonary blastomycosis.

PRIMARY BLASTOMYCOSIS OF THE SKIN

Dermal lesions appear much more frequently in patients with blastomycosis than in patients with tuberculosis, histoplasmosis, or coccidioidomycosis but less frequently than in patients with sporotrichosis. About 30% of our patients with blastomycosis have had dermal lesions.

The disease, blastomycosis, was discovered by dermatologists and assumed for some years to be limited primarily to the skin. The original clinical diagnosis on the first recognized case of blastomycosis was scrofuloderma. The second case, reported in 1896, by Gilchrist and Stokes[1] was described as "pseudo-lupus vulgaris." This patient was not obviously ill but had disfiguring lesions of the ears, nose, and face, which had developed slowly over the previous eleven years.

DAVID T. SMITH, M.D. *is chairman of the Department of Preventive Medicine, Duke University School of Medicine, Durham.*

Nearly all of the first 50 published cases were from dermatology clinics. It was assumed that the spread of localized lesions from one side of the face to the ears, nose, wrist, and ankle was a direct inoculation from the contaminated fingers of the patient. Stober[2] watched two of his patients spread their disease in this manner and demonstrated Blastomyces dermatitidis in the detritus cleaned from beneath their fingernails.

In 1908, Montgomery and Ormsby[3] recognized the primary systemic form of blastomycosis and isolated the organism from the blood of two patients. They also pointed out that the skin lesions which developed in association with the systemic cases differed in location and in evolution from the original dermal cases. These lesions were scattered over the trunk, arms, legs, and face in a haphazard manner rather than being confined primarily to the face and extremities. In the initial stages of development, these new lesions were in the subcutaneous tissues but evolved into dermal lesions after breaking through the epidermis and invading this layer of the skin. Lesions developing in this manner became indistinguishable from those which evolved from a pimple in the epidermis. The early investigators also recognized the rather benign course of the "primary" cutaneous blastomycosis in contrast to the rapidly fatal course in patients with primary systemic blastomycosis and secondary cutaneous manifestations.

In 1955 Wilson, Cawley, Weidman, and Gilmer[4] attempted to refine the definition of primary cutaneous blastomycosis and limit it to those cases which show a local chancre-like lesion filled with organisms and accompanied by enlargement of the regional lymph nodes. The model for this type of lesion can be found in accidental inoculation tuberculosis on an extremity or a spontaneous sporotricholic infection of an extremity. In a thorough search of the literature, Wilson and his associates[4] found only four cases which met these criteria. In all four instances, the organisms were introduced into the deep tissues of an extremity with trauma. All four of these patients made a spontaneous recovery and have remained well for years.

It is obvious that a patient presenting a local lesion accompanied by gross enlargement of the regional lymph nodes can be diagnosed as a primary infection, but the author was reluctant to accept the converse of this statement and deny the diagnosis of a primary dermal infection when the lymph node element was absent. It was decided to review the variety of skin lesions found in tuberculosis and in sporotrichosis in the absence of and in the presence of allergy and relative immunity. The latest editions of six of the best known textbooks on dermatology were consulted, and it was found that there was general agreement that the great variety of tuberculous lesions of the skin were the result of varying degrees of allergy and immunity, although these specific words were not always used in the descriptions. The variety of skin lesions induced by the tubercle bacillus and its products is shown in the table.

When tubercle bacilli are introduced into a cut or by a needle into the skin of an extremity, in a healthy individual who has a negative tuberculin test, a series of changes occur which are analogous to the well-known primary complex in the lungs. The local lesion develops slowly into an indolent chancre-like lesion; lymphangitis with nodule formation occurs in the drainage tract to the regional lymph nodes which become enlarged about the time the tuberculin test becomes positive.

Most spontaneous primary tuberculous infections of the skin are in children and occur on or about the nose and face. The source of the disease is usually droplet infection from the cough of a tuberculous relative or direct inoculation by rubbing the nose or face with a handkerchief which has been contaminated with microscopic particles of sputum containing tubercle bacilli. The lesion induced in this manner may follow any one of three divergent courses. The tubercle bacilli may escape from the regional lymph nodes in numbers, invade the internal organs, and cause a fatal case of disseminated tuberculosis. This is the rarest of the three possible results. The most common outcome is healing of lesion. Tubercle bacilli which were in abundance in both the local lesions and in the lymph nodes are reduced to a few scattered organisms when allergy to tuberculin appears. The part played by the allergy itself and that by the accompanying immunity has never been settled. The enlarged lymph nodes disappear and the skin heals with a pliable scar. The healing process is slow and may require years without specific therapy and many months with such therapy. The third type of development is the production of the characteristic granulomatous reaction known as lupus vulgaris which is a much more chronic disease than the healing primary infection described above. This type of reaction seems to appear when there is a certain balance in the degree of allergy and immunity suggesting that the allergy was inhibiting the favorable effect of the immune mechanism.

Lupus vulgaris may develop [1] in a patient who originally presented the characteristic picture of a primary infection with enlarged lymph nodes, [2] in a patient who was known to have a positive tuberculin test before the skin was infected, or [3] in a patient who has a primary infection with a very small number of bacilli in the most superficial layers of the skin so that allergy and relative immunity appear before the regional lymph nodes become enlarged. Dermatologists are familiar with the sequence of events when the primary chancre-like lesions become granulomatous and the regional lymph nodes return approximately to their original size. They are also familiar with the inoculation of the skin of the face in an individual who already has allergy and some immunity. Under these circumstances, the usual result is a severe local reaction with healing or the more unusual result of developing the lupus vulgaris type of reaction. In neither instance are the regional lymph nodes enlarged. The belief that lupus vulgaris can develop from a primary infection is to a large degree theoretical, but a basis for this theory has been proved by actual inoculation of the skin of man with tubercle bacilli in the attempt to produce immunity with bacille Calmette Guérin (BCG) vaccine.

Originally, BCG vaccine was given to newborn infants by mouth in an attempt to immunize them against tuberculosis. But, positive tuberculin skin tests following these feedings were irregular in occurrence. The next step was the inoculation of the BCG subcutaneously, usually on the leg. This resulted in the production of a local abscess and enlargement of the regional lymph node which often broke down and formed a sinus. This reaction is the analogue of accidental infection on an extremity in a tuberculin negative individual. In the third procedure, the BCG was inoculated intracutaneously. A local ulceration appeared at the site of the inoculation, but the regional lymph nodes were rarely enlarged and almost never broke down. In rare instances, the balance of immunity and allergy was such that the local superficial dermal infection developed into a lesion with the clinical and pathological characteristics of lupus vulgaris. However, the intradermal inoculation in infants and young children produced many instances of lymph node enlargement in contrast to the rare occurrence of this complication in adults. The development of these lesions in infants led to the fourth procedure of multiple puncture, where the bacilli were inoculated even more superficially by needles or tines. This method of inoculation gave a number of minute skin reactions but good conversion of the tuberculin with few or no complications in the lymph nodes. This series of observations suggests that the regional lymph nodes may or may not be enlarged, even with a primary infection, if the dose is small and the inoculation very superficial.

Primary pulmonary infections with Sporotrichum schenckii do occur but are rare or rarely recognized, or both. Systemic or generalized infections are more common than pulmonary, but both together would not account for more than 10% of the known cases. Primary dermal lesions are obviously the most common manifestation of sporotrichosis in man. The infections are usually on an extremity and most often are introduced by the prick of a thorn, a splinter, or a briar. It is not surprising that the characteristic symptoms include the local chancre, the lymphangitis, and the enlarged regional lymph nodes. However, dermal sporotrichosis can occur without the lymphatic elements and in the absence of enlargement of the regional lymph nodes. There were no systemic cases among the 650 patients studied by DuToit in native workers in the gold mines of South Africa. DuToit recognized a superficial type of infection without the lymphangitic and adenitic components.[5] He stated, "Practically the only type seen on the face, and then very frequently on the forehead between the eyes, is the warty or papillomatous type of primary. This is a superficial lesion and very difficult to distinguish from a papilloma. It may exactly simulate the appearance of blastomycosis. However, these primaries may occur on any part of the body with the exception of the feet and pelvic girdle and are frequently multiple both in distribution and type." Dr. L. M. Smith reported from Texas a small series of proved sporotrichosis infections of the face where the lymphangitic and adenitic elements were absent.[6] Our dermatology department has seen instances of granulomatous lesions on the extremities without lymphangitic or adenitic elements which were shown by biopsy and culture to be sporotrichosis. These patients were usually referred to our hospital as probable cases of neoplasia.

A modification of Sutton's classification of tuberculous lesions of the skin is shown in the table. The primary tuberculosis complex type seems to be most frequent in sporotrichosis, next is tuberculosis, and rarest is blastomycosis.

Scrofuloderma-type lesions represent a secondary infection of the skin from an infected bone or lymph node. It is most common in blastomycosis, next in tuberculosis, and rarest in sporotrichosis. The tuberculosis cutis orificialis may occur in sporotrichosis but has not been reported

SUTTON'S CLASSIFICATION OF TUBERCULOUS LESIONS OF THE SKIN*

Localized types

1. Primary tuberculous complex in the skin
2. Scrofuloderma
3. Tuberculosis cutis orificialis
4. Tuberculosis verrucosa cutis
5. Lupus vulgaris

Hematogenous tuberculosis

1. Acute miliary tuberculosis of skin and internal organs
2. Multiple disseminated tuberculosis of the skin with localized caseation
3. Tuberculids with hypergic immunity
    a. Lichen scrofulosorm
    b. Papulonecrotic tuberculids

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*Sutton's *Diseases of the Skin*, 11th ed., St. Louis: C. V. Mosby Co., 1956, pp. 328-329.

for North American blastomycosis, although something like this is common in South American blastomycosis.

Tuberculosis verrucosa cutis occurs more often in patients with pulmonary tuberculosis who infect their own skin with bacilli from their sputum. This type of lesion is not very common in tuberculosis but relatively common in blastomycosis. It has not been reported for sporotrichosis.

Lupus vulgaris has many minor variations in man. Sutton shows an illustration in the eighth edition of his *Diseases of the Skin* where a solid and presumably rather early lesion occurs on one buttock and an older larger lesion on the other buttock. The larger lesion has a verrucous spreading edge with a flat, paper-like healed area in the center. This type of lesion is very common in blastomycosis but not recognized in sporotrichosis.

It should be emphasized that the tuberculosis verrucosa cutis and the lupus vulgaris type of lesions can develop either as a form of a primary infection or more characteristic as a secondary superficial inoculation in the presence of allergy and relative immunity to either tuberculosis or blastomycosis. In contrast, the primary complex in the skin must be from a primary and the scrofuloderma must be from a secondary underlying lesion. The dermal lesions in systemic cases of blastomycosis are indistinguishable in appearance from the primary epithelial inoculation type, but the history of the two lesions is quite different. The primary skin lesion begins as a tiny pimple in the superficial layer of the skin while the secondary lesions begin as subcutaneous abscesses which rupture through the skin and then infect the superficial layers.

The hematogenous infections are shown in the table. Miliary blastomycosis of the skin is indistinguishable clinically from miliary tuberculosis of the skin. Multiple disseminated tuberculosis of the skin with localized caseation has not been reported for blastomycosis probably because the degree of allergy in blastomycosis is not sufficient to cause local caseation in the lesions. The tuberculoid type of skin lesions, seen in tuberculosis and in some of the dermatomycosis, has not been reported in blastomycosis because of the poor grade of allergy developed by the patients with blastomycosis.

SUMMARY

The fungal diseases mimic tuberculosis in many ways. The primary complex in tuberculosis is duplicated almost exactly in histoplasmosis, except there is even more calcification in the lungs and hilar glands. Coccidioidomycosis produces some hilar adenopathy but less calcification than tuberculosis. Blastomycosis occasionally produces enlarged hilar lymph nodes but never calcification. The reinfection syndrome with upper lobe cavities is obvious in histoplasmosis but reinfection coccidioidomycosis or blastomycosis has not been observed.

Both primary and reinfectious lesions of the skin are found in tuberculosis, sporotrichosis, coccidioidomycosis, and blastomycosis. These dermal lesions are found most frequently in sporotrichosis, next in blastomycosis, sometimes in coccidioidomycosis, and least frequently in tuberculosis.

There is difference of opinion at the present time concerning the definition of primary blastomycosis of the skin. One school of dermatologists would limit the designation of primary to those cases which have [1] a well-defined, local, chancre-like primary lesion, [2] a spreading lymphangitis, and [3] a regional lymph node enlargement. This corresponds to the classical primary tuberculosis of the skin, but only four cases of blastomycosis fitting this description have appeared in the literature. The author objects to this limited definition of primary infection of the skin and has presented evidence that primary infections of the skin in tuberculosis, blastomycosis, and sporotrichosis can and do occur in numbers where the lymphatic component of the complex is absent. He has shown that BCG regularly gives the entire primary complex when injected subcutaneously in the leg but most often a lesion without a detectable lymphatic component when introduced intradermally in adults or by multiple puncture in infants.

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Beau's Lines in a Case of Myelomatosis

HANS ABERG, M.D., and DAVID CRAIG, M.D.

Umeå, Sweden, and Minneapolis, Minnesota

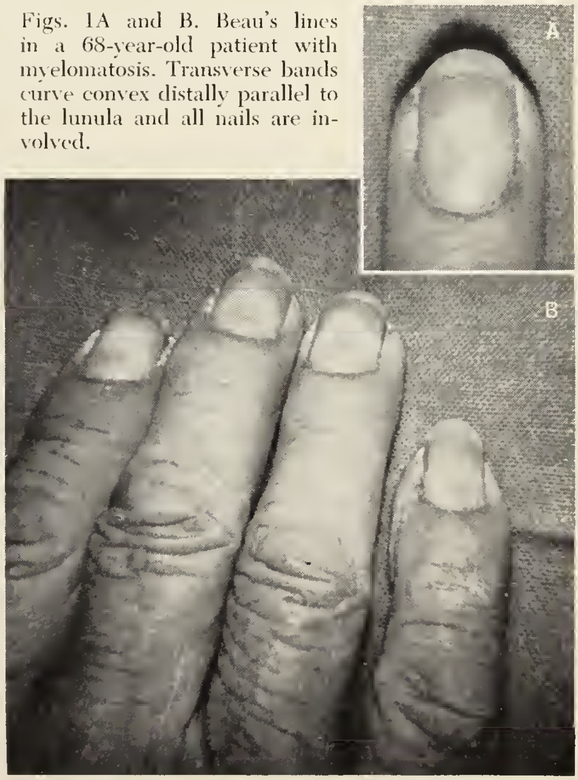
THE FRENCH PHYSICIAN, Joseph Honoré Simon Beau (1806 to 1865) was the first to describe a certain disorder of the nails occurring in some systemic diseases. These so-called Beau's lines are transverse bands which are curved convex distally.[1,2] They are parallel to the lunula of the nail. The Beau's lines represent a temporary damage of the growth of the nail due to a sudden arrest of the function of the nail matrix. This occurs in some systemic diseases of mostly transient character such as cardiac infarction, cholecystitis, or pneumonia or when there is a sudden change in a long-lasting, wasting disease as, for example, an acute exacerbation in a chronic glomerulonephritis.[3,4] As a curiosity, we can mention that it has been described after severe seasickness. Another characteristic feature of this disorder of the growth of the nails is that it usually involves all the nails. This is in contrast to those bands which occur on one or two of the nails due to trauma or manicuring. These traumatic bands are also curved in a different way, namely, concave distally.

A few cases with these Beau's lines have been published and this nail disorder is pictured in some dermatology textbooks. In the case presented here, the Beau's lines were unusually prominent and of interest from the etiologic point of view.

CASE REPORT

A 68-year-old man had a transurethral resection for benign prostate hypertrophy in 1960. He also had a history of gallbladder disease and asthmatic bronchitis. He was hospitalized Oct. 10, 1964, with a two- to three-months' history of pain in the back and in the left upper quadrant of his abdomen and with intermittent nausea. There were no significant findings on physical examination. Laboratory studies on admission showed hemoglobin, 10.1 gm. percent; white blood cell count and differential, normal; and blood urea nitrogen, 27 mg. percent. An intravenous pyelogram showed poor renal function, and, during the next two weeks, the blood urea nitrogen rose to 125 mg. percent. Because of the possibility of an acute renal failure, the patient was transferred to the Bethesda Lutheran Hospital, St. Paul, where hemodialysis was carried out fifteen times. His condition, however, continued to worsen. Subsequent studies showed a sedimentation rate, 138 mm. (Westergren); serum protein, 8.5 gm. percent of which 3.8 gm. percent was gamma globulin. Plasma electrophoresis revealed a homogenous band in the gamma-2 region. A kidney biopsy was consistent with myelomatosis with multiple myeloma casts. He died Dec. 2, 1964. An autopsy was not obtained.

During the entire stay at the Bethesda Lutheran Hospital, the Beau's lines were present (see Figs. 1A and B).



Figs. 1A and B. Beau's lines in a 68-year-old patient with myelomatosis. Transverse bands curve convex distally parallel to the lunula and all nails are involved.

HANS ABERG *is a medical fellow, University Hospital, Umeå, and* DAVID CRAIG *is clinical associate professor, University of Minnesota, Minneapolis.*

DISCUSSION

In enduring, wasting diseases, there often appear longitudinal lines on all nails such as also may accompany arsenic intoxications. These could not be observed in this patient but, instead, he showed very typical Beau's lines. If these were due to his myelomatosis per se or to the complicating uremia is of only theoretical interest. The time of appearance, together with the usual slow growth of the nails, suggest the myelomatosis itself as the causative factor. On the other hand, it is very likely that the patient's renal insufficiency was of longer duration, which could explain his complaint of nausea before admission. In other words, the admission blood urea nitrogen of 27 mg. percent may not have been representative of his renal function. A strong support for the last statement is the intravenous pyelogram, which showed poor renal function at the time of admission. In that case, the uremia might be the cause for his Beau's lines.

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The Weak Patient—(Continued from page 498)

George C. Flora, M.D., and A. B. Baker, M.D.

ously consider a diagnosis of metastatic carcinoma. The lesion invariably shows a progressive course over a period of observation. The clinical entity is substantiated if one obtains a history of weight loss, signs and symptoms of a primary neoplastic lesion of any organ, or X-ray evidence of bony metastases. Examination of the patient will frequently reveal marked focal pain over the metastatic lesion; this is associated with a positive Patrick's sign if the lesion lies within the lumbosacral region. Lumbar puncture shows evidence of spinal block—decreased reflection of intracranial pressure changes transmitted to the needle site (Queckenstedt)—and with an increase of cerebrospinal protein levels.

Treatment of this condition is immediate decompression. If the disorder is permitted to persist in excess of two to six hours, permanent residual is to be expected. Following decompression, deep X-ray to the metastatic site and removal of the primary lesion may be indicated.

GRADUAL ONSET IN OLD AGE

Amyotrophic lateral sclerosis. This condition is the most common cause of slowly progressive lower motor neuron deficit in patients more than 55 years. The symptom complex does not differ from that described for the younger age groups. Treatment and prognosis are the same for all ages.

Primary and Secondary Blastomycosis of the Lungs and Skin—

David T. Smith, M.D.

(Continued from page 502)

When the infection spreads from an infected bone or lymph node to the overlying skin, there is a secondary infection of the skin. This type of lesion occurs in tuberculosis and sporotrichosis but more often in coccidioidomycosis and most often in blastomycosis because the bones are more frequently infected in these diseases. A common type of secondary dermal lesion occurs in patients with systemic blastomycosis where there may be single but more often multiple subcutaneous lesions induced by dissemination through the bloodstream. These are easily recognized if a good history can be obtained because the epidermis is not involved until the subcutaneous lesion breaks through the skin. However, subsequently, the dermal lesions became indistinguishable from a primary infection where the initial lesion began as a small pimple in the epidermis.

Patients who have had a subclinical infection with the tubercle bacilli or with B. dermatitidis may develop dermal lesions without associated lymphatic spread when the corresponding organism is introduced into the superficial layers of the skin.

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Long-Term Follow-up of Bronchiectasis

ARCHIE FINE, M.D., and GERALD L. BAUM, M.D.

Cincinnati

SINCE THE ADVENT of the use of antibiotics and chemotherapeutic agents, it appears that the incidence of bronchiectasis is falling. Certainly, the clinical impression seems valid that patients having extensive and severe bronchiectatic lesions are not being seen with the same frequency with which they were being encountered fifteen or more years ago. Nevertheless, bronchiectasis still represents a serious clinical problem and, in many instances, challenges the judgment of the physician. The major problem confronting most physicians is whether or not resectional surgery is indicated. It is not the patient with a large localized area of bronchiectasis, expectorating foul-smelling sputum, who presents a problem. Neither is the case particularly vexing that manifests recurrent hemorrhage from a single area of the lung. In these instances, the indications for resection are clear. However, the real enigma is the patient who has a slowly resolving episode of pneumonia, or recurrence of pneumonia in a single area of the lung, who has a bronchogram which shows cylindrical dilatation. This patient is usually considered for surgery unless there are functional abnormalities which preclude thoracotomy.

The enthusiasm for surgery has been somewhat tempered in these situations by several interesting circumstances.[1] In the first place, the natural history of bronchiectasis is not well understood. It is not known whether or not removing a single obvious area of bronchiectasis in any way alters the course of the patient's life. It is conceivable that the defect that leads to bronchiectasis may be generalized and that the area we observe on our bronchogram may only represent the most flagrant expression of something which exists all through the patient's lungs. If this is the case, it might well stay the hand of the surgeon, since the removal of one area of the lung might soon be followed by the appearance of similar pathology in another. Another circumstance which makes the picture more confusing is that in recent years cylindrical dilatation of bronchial radicals has been recognized as a reversible phenomenon. During acute pneumonia, in the course of partial bronchial obstruction with collapse, and in lungs which have been distorted by emphysematous areas elsewhere, bronchial dilatation of a cylindrical nature may be observed. Where follow-up bronchograms have been done, return of the bronchial lumen to normal caliber has been observed.[2,3] It seems generally agreed, therefore, that only marked saccular bronchiectasis invariably is irreversible.[3]

STUDY OF CURRENT MATERIAL

Source of cases. During World II, one of the authors (A.F.) was stationed at an Air Force training center where candidates for flying training received a comprehensive physical examination. The latter included stereoscopic 4- by 5-in. chest X-rays. All of these men had had a physical examination before arrival at the center. Many had had chest X-rays and had been on active duty; some had been overseas.

A total of 156,000 men were examined.[4] A variety of lung lesions was found. Those men showing exaggerated lung markings with or without infiltrate, segmental or lobar collapse, or pleural changes were admitted to the hospital for study. Of 638 men with nontuberculous infiltrations, the majority cleared rapidly. About 100 did not clear. These men were further studied by bronchography. Forty-one were found to have bronchiectasis, either saccular or cylindrical. It should be noted that the lungs were not completely examined. Once the fluoroscopic examinations revealed the presence of bronchiectasis, the instillation of iodized poppy-seed oil (Lipiodol®) was terminated, and chest X-rays were taken. For this reason, in some instances only one side was examined. Because of the variety of symptoms and the apparent well-being of these men, questionnaires were sent to them after they had returned to civilian life. Inquiries

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ARCHIE FINE *is radiologist, Jewish Hospital, Cincinnati, and* GERALD L. BAUM *is chief, Pulmonary Disease Section, Veterans Administration Hospital, Cleveland.*

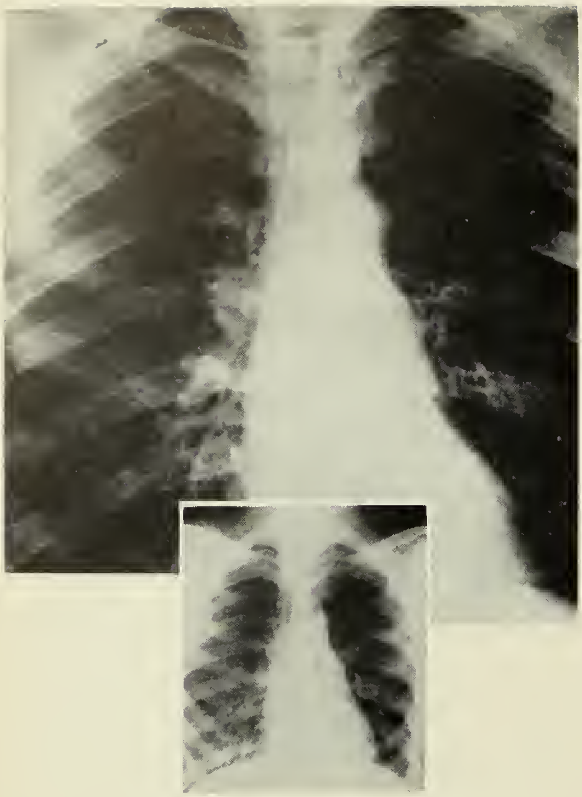

Fig. 1. Posteroanterior chest X-ray showing collapsed left lower lobe behind the heart. [Inset] Induction film shows same finding.

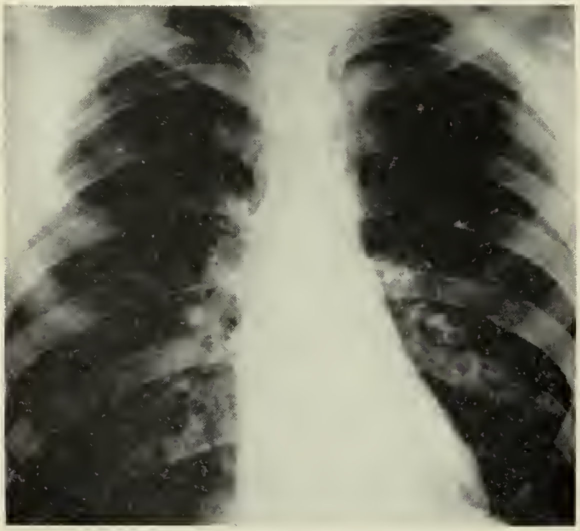

Fig. 2. Bronchogram showing saccular bronchiectasis

concerning their health, work habits, and so forth continued through 1947, when the study was terminated.[5]

Present follow-up. Our interest was renewed in 1962 when a letter was received by one of us (A.F.) from one of the men requesting information because his pension was being terminated. His history is of general interest.

CASE REPORT

This man was inducted into the service in 1942. He arrived at the Classification Center where he was X-rayed. This revealed a collapsed left lower lobe. The induction film was later obtained and showed the same findings. There were also areas of infiltration in the right lung. Lipiodol® instillation revealed extensive saccular bronchiectasis (Figs. 1 and 2). A bronchogram was not made of the right side. Subsequent X-rays have shown the left lobe still collapsed. This man has been in excellent health and has continued to work.

Because of this incident, it was thought that some interesting information might be obtained if the subsequent history of the men in the original study[5] could be obtained after a lapse of twenty or more years. Of the 41 individuals, only 37 had been followed previously. Of these 37, a correct address or follow-up could not be found on 8. Of the remaining 29, responses were obtained from 24. Three were known to be dead, and current information was obtained from 21. The information obtained from this letter survey serves as the basis for this report.

A form letter was sent to each veteran, and the following 5 questions were asked: [1] Are you working at the present time and, if not, is it because of lung trouble? [2] Have you had an operation on your lungs? [3] Do you have cough and/or do you raise much phlegm? [4] Have you coughed up blood? [5] Have you developed asthma or shortness of breath?

In addition to this questionnaire, a request was sent to the individual asking for a report from his physician on his latest medical checkup and for his most recent chest X-rays. This latter request was not made unless there was a positive answer to the original form letter. For purposes of categorizing the cases, the old X-rays were reviewed and the results were tabulated.

RESULTS (TABLES 1 AND 2)

Information was available on 2 of the 3 patients known to be dead. One patient was hospitalized in 1943 with evidence of a rib resection on the right and with a stroke manifested by a right hemiplegia. He died a few hours after admission, never having regained consciousness. No autopsy was done, so it is not known whether or not the stroke resulted directly from lung disease. One patient died in an automobile accident, and the cause of death of the third was unknown.

Of the 21 patients who responded to the request for information, 20 were working at the time of correspondence, in the fall of 1962. Four of the 21 had had pulmonary resections. One of this group was the patient who was not working.

TABLE 1

RESULTS OF FOLLOW-UP LETTERS SENT TO 37 PERSONS WITH BRONCHIECTASIS

A. Responses obtained		24
Alive	21	
Dead	3	
B. Causes of death		
Bronchiectasis complication (probable)		1
Accident unassociated with bronchiectasis		1
Unknown		1
C. Working at time of follow-up		20
D. Pulmonary resection		4
Right upper lobe		1
Left lung (extent unknown)		3
E. Symptoms at time of follow-up		
None		7
Minimal		10
Moderate to severe		4
F. Type of symptoms		
Cough and sputum		11
Hemoptysis (minimal in all cases)		5
Dyspnea (minimal to moderate)		5

TABLE 2

TABULATION OF ORIGINAL X-RAY FINDINGS IN 21 LIVING PATIENTS

Cylindrical bronchiectasis	19
Bilateral	6
Saccular bronchiectasis	6
Bilateral	1
Cylindrical and saccular bronchiectasis	4
Collapsed lobe	1

Seven of the 21 patients were without symptoms. Eleven of the 21 patients still manifested cough and sputum, including 3 of the 4 patients who had had pulmonary resection. Hemoptysis had been observed by 5 patients, only 1 of whom had had a resection. Dyspnea on exertion was complained of by 5, including only 1 who had had a resection.

DISCUSSION

Despite the relatively small number of patients in this series, it seems worthwhile to bring this information to the attention of the profession at large, because it raises some fairly provocative points concerning the treatment of bronchiectasis. Considering this as a group of 24 patients with approximately twenty-year follow-up, the benign nature of the disease is remarkable. It is also of interest that all but 1 of the 21 living patients are working. Pulmonary resection, having been done only four times in the entire group, does not seem to have added materially to the clinical well-being of these people. There are many arguments which can be used to justify or to decry the use of surgery as a method of treatment in bronchiectasis. By no means would the present authors suggest that surgery is not indicated in certain circumstances. However, we feel it should be emphasized that in a long-term follow-up study such as this the point is clearly made that the prognosis of patients with bronchiectasis of a limited degree is good, with or without surgery. This has been the experience of others.[6,7]

It must be kept in mind that though these patients had had their bronchiectasis discovered before the antibiotics era, the use of these drugs during the past seventeen to eighteen years has undoubtedly influenced the clinical course of these patients. In fact, several of them might have sustained serious infections which, without antibiotics, would have gone on to uncontrolled suppuration. Assuming appropriate use of antibiotics, this small series of cases with long-term follow-up provides information concerning the natural history of bronchiectasis of limited extent which should be useful in evaluating the prognosis of this type of disease.

SUMMARY

Forty-one cases of bronchiectasis were found during the examination of 156,000 flying training applicants 18 to 25 years of age. Thirty-seven had been followed up to 1947, and information about 24 was obtained approximately twenty years after the diagnosis was made. Twenty-one of the 24 were alive, and 20 of the 21 were working at the time of latest follow-up. Only 4 had had pulmonary resections, and 7 were without symptoms. The generally benign nature of this type of bronchiectasis is stressed.

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Transactions of the North Dakota State Medical Association

TRANSACTIONS OF THE TWENTIETH ANNUAL MEETING OF THE WOMAN'S AUXILIARY TO THE NORTH DAKOTA STATE MEDICAL ASSOCIATION

Fargo, North Dakota, April 29, 30 and May 1, 1966

The Twentieth Annual Meeting of the Woman's Auxiliary to the North Dakota State Medical Association was held in the Regency Room of the Town House in Fargo at 9:30 A.M., Saturday, April 30, 1966, with Mrs. M. A. K. Lommen, State President, presiding.

Mrs. E. O. Hieb, State President-Elect, led our Pledge of Loyalty. The Invocation was given by Mrs. L. G. Pray.

Mrs. G. U. Ivers welcomed all the members to this State Meeting in Fargo. Mrs. S. J. Thakor gave a generous response to the First District.

Mrs. Lommen introduced Dr. Joseph D. Craven, President of the North Dakota State Medical Association. He brought greetings from the State Medical Association and praised the Woman's Auxiliary for all the help given in such worth while projects as the Medical Auxiliary Student Loan Fund.

Mrs. Frank M. Melton was in charge of the Memoriam for Mrs. Paul Burton, Mrs. R. O. Goehl, and Mrs. Robert McFadden. Mrs. J. R. Goff, violinist, accompanied at the piano by Mrs. N. F. Goltz presented a musical selection.

Mrs. Willard C. Scrivner, North Central Regional Vice President from East St. Louis, our National Auxiliary guest was introduced by Mrs. Lommen.

Mrs. R. J. Ulmer, Recording Secretary, called Roll. Answering were Mrs. M. A. K. Lommen, President; Mrs. E. O. Hieb, President-Elect; Mrs. L. G. Pray, Second Vice President; Mrs. R. J. Ulmer, Recording Secretary; Mrs. J. J. Moses, Corresponding Secretary; Mrs. R. M. Berg, Treasurer; Mrs. H. Evans, Historian; Mrs. G. U. Ivers, A.M.A.E.R.F.; Mrs. P. F. Klosterman, Health Careers; Mrs. Paul Ahlness, By-Laws; Mrs. S. J. Thakor, Mental Health; Mrs. R. E. Mahowald, Disaster Preparedness; Mrs. K. N. Amstutz, Safety; Mrs. C. J. Fercho, Publicity; Mrs. R. O. Saxvik, Community Service; Mrs. J. A. Lambie, *News, Views and Cues*—Business and Circulation Manager; Mrs. W. Hanewald, Finance; Mrs. P. B. Curtis, Seventh District President; Mrs. J. D. Craven, Eighth District President; Mrs. G. H. Holt, Seventh District Councilor; and Mrs. R. W. McLean, Tenth District Councilor. A quorum was present.

Mrs. G. U. Ivers moved to accept the minutes of the 1965 Convention as published in the Journal-Lancet. The motion was seconded and carried.

Mrs. Lommen announced that the 43rd Annual Convention of the Woman's Auxiliary to the A.M.A. would meet June 26-30, Drake Hotel, Chicago, Illinois. The Annual Fall Conference will be held October 2-5, Drake Hotel, Chicago, Illinois. The Regional Workshop (North Central) will be held October 4-5, Drake Hotel, Chicago, Illinois. The Chairmen of A.M.A.E.R.F.; Community Service; Legislation; Membership; Mental Health; and Rural Health are requested to attend.

Mrs. R. W. McLean presented the Registration Report: Executive Board, thirty-eight; fourteen delegates; one alternate delegate; and a total attendance of sixty.

Parliamentarian, Mrs. R. D. Schoregge read her report.

In the President's Report, Mrs. Lommen recognized the President-Elect, Mrs. E. O. Hieb.

Mrs. E. O. Hieb read the membership report pointing out that most Districts have not accepted the 100% team membership plan with their husbands. Our auxiliary membership has increased. Seventh District has enacted 100% team membership.

It was moved and seconded to adopt the agenda. The motion carried.

WASAMA report was read by Mrs. R. J. Ulmer. It related special projects and net profits.

Mrs. H. Evans presented the Historian's Report. She stressed that we should seek important action other than the lives and doings of our children.

A.M.A.E.R.F. reported that we have improved our contributions but we could do better. Mrs. G. U. Ivers went on to state that one doctor and his wife gave a fifty dollar gift through the Auxiliary. This does give our Auxiliary more credit.

Health Careers Report was read by Mrs. P. F. Klosterman. She told of various District projects. The State Rally will be held this Fall in Bismarck.

Proposed changes to the By-Laws were read by Mrs. Paul Ahlness. She moved that these amendments be adopted. The motion was seconded and carried.

The Mental Health Report was given by Mrs. S. J. Thakor. She distributed Information Packets for additional help to the Districts.

The Legislation Report was read by Mrs. R. J. Ulmer. There was not much activity, but Fall should bring more.

Information as to the depository for the drug articles for International Health Activities was given by Mrs. Lommen.

Safety Chairman, Mrs. K. N. Amstutz, reported and recommended that we again work with our local groups to assist in any possible way.

Publicity Chairman, Mrs. C. Fercho read her report.

Community Service Chairman, Mrs. R. O. Saxvik reported on various projects, such as working with churches, schools, hospitals and community club groups.

News, Views and Cues Report was given by Mrs. J. Olson.

Treasurer, Mrs. R. M. Berg gave her report and requested that dues be sent in before the cut-off date of February 15th.

Mrs. Klosterman presented several bills and moved that they be allowed. The motion was seconded and carried.

The Medical Auxiliary Student Loan Fund Report was given by Mrs. J. Moses, in the absence of Mrs. M. Poindexter. Mrs. Moses moved to rescind the vote cast at the Fall Board Meeting to send all receipts to the Medical Auxiliary Student Loan Fund through A.M.A.E.R.F, directed to U.N.D. Medical School. Upon receipt these were to be transfered to the Auxiliary Loan Fund. The motion was seconded and carried. She also moved that all Student Loan Fund money should be sent from our Student Loan Fund Chairman directly to Dean Harwood or Dr. Arnason, University of North Dakota Medical School. This motion was seconded and carried. A deficit exists in the Fund and this action would avoid delay and make this year's contributions immediately available for student loans.

Mrs. E. O. Hieb moved that the $25.00 minimum balance in the Medical Auxiliary Student Loan Fund (as per original agreement) be eliminated. The motion was seconded and carried. Mrs. Hieb also moved that a loan granted to a student shall be due one year after the completion of his/her internship. The motion was seconded and carried.

The Finance Report was given by Mrs. W. Hanewald. The motion was made, seconded and carried that the Budget Report be accepted.

Mrs. V. J. Fischer, in the absence of Mrs. C. Smith, presented the Nominating Committee Report: President, Mrs. E. O. Hieb; President-Elect, Mrs. L. G. Pray; First Vice President, Mrs. H. Evans; Second Vice President, Mrs. C. London; Recording Secretary, Mrs. Paul Ahlness: Treasurer, Mrs. R. Berg. The motion to accept the slate of officers was approved and carried. A unanimous voice vote was cast and the slate elected.

The meeting was recessed for the noon luncheon.

Mrs. Lommen called the meeting to order.

Disaster Preparedness Chairman, Mrs. R. E. Mahowald brought up the fact that Civil Defense has had no action. There has been no response from any District in North Dakota.

The Reports of the District Presidents were read and are on file.

Mrs. Lee Christoferson presented the final attendance report of ninety-two.

The following Resolution directed from the House of Delegates to the North Dakota State Medical Association to Mrs. M. A. K. Lommen and her successor was received:

RESOLUTION

WHEREAS, the ladies of the Women's Auxiliary to the North Dakota State Medical Association, through devoted enthusiasm and continuous efforts over the years have contributed diligently to the Medical Auxiliary Student Loan Fund of the Medical School of the University of North Dakota, and more recently to the American Medical Association Education and Research Fund, and

WHEREAS, these funds have enabled many medical students to complete their medical education, and

WHEREAS, the local Auxiliary Societies throughout the State have participated in many other commendable projects which reflect credit to their organization and to the Medical Profession,

NOW, THEREFORE, BE IT RESOLVED that the House of Delegates of the North Dakota State Medical Association convey to the Women's Auxiliary our appreciation and thanks for their excellent work, and

BE IT FURTHER RESOLVED that a copy of this Resolution be directed to Mrs. M. A. K. Lommen, and her successor.

Unfinished Business:

A motion was made, seconded and carried that the Journal-Lancets carrying the Convention Reports be bound every five years. This action directs the Records of the Thirteenth, Fourteenth, Fifteenth, Sixteenth and Seventeenth Annual Meetings to the bindery.

Special Committee Report—Nurse Loan Fund. A motion was made, seconded and carried that this committee be continued. Edna Moses, Zoe Smith and Mary Lommen will comprise the Committee.

A motion was made, seconded and carried that a copy of each issue of *News, Views and Cues* be sent to the Recording Secretary to be kept in a folder with the Journal-Lancet records of the Auxiliary.

A motion was made, seconded and carried that the Auxiliary order new stationery through the Office of the Executive Secretary.

A motion was made, seconded and carried to request the Office of Executive Secretary to cut stencils of Auxiliary By-Laws and to send these to the District Presidents to be distributed to the members in good standing.

Mrs. Willard C. Scrivner installed the new officers: President, Mrs. E. O. Hieb; President-Elect, Mrs. L. G. Pray; First Vice-President, Mrs. H. Evans; Second Vice-President, Mrs. C. London; and Recording Secretary, Mrs. Paul Ahlness.

Mrs. Lommen pinned Mrs. E. E. Hieb, our new State President; in return Mrs. Hieb pinned Mrs. Lommen with the Past President's pin.

Mrs. R. D. Schoregge presented Mrs. Lommen with a gift in appreciation from the Sixth District.

It was moved and carried to adjourn the meeting. The meeting was adjourned.

MRS. R. J. ULMER, *Recording Secretary*

Woman's Auxiliary to the American Medical Association 1966 Convention Rules of Order

1. The registration committee shall report at the opening and closing business meetings, or when directed to to do so.
2. Delegates shall be furnished badges by the registration committee when they register and are requested to wear them during all general meetings of the convention.
3. A delegate shall represent only one auxiliary and be entitled to only one vote.
4. Delegates are requested to attend all business meetings of the convention.
5. No delegate shall be entitled to the floor unless she rises, addresses the presiding officer and gives her name and the name of her district auxiliary.
6. Reports of the district auxiliaries shall be limited to two minutes and shall be read by a representative of the auxiliary.
7. A motion shall be written, signed by the mover and presented to the Recording Secretary.
8. Announcements and general interest messages shall be made from the platform. Notes and messages shall be passed by pages.
9. Visitors are welcome at the general meetings and are requested to register.

MRS. R. D. SCHOREGGE, *Parliamentarian*

Convention Report

With a Spring flower theme our luncheon was served in the Embassy Room of the Town House, April 30, 1966, at 12:30 P.M. Mrs. E. O. Hieb opened the meeting and introduced Mrs. Lee Christoferson, Chairman; Mrs. G. U. Ivers, First District President; Mrs. R. J. Ulmer, Recording Secretary; Mrs. M. A. K. Lommen, outgoing President; Mrs. R. M. Berg, Treasurer; Mrs. Lester Wold and Mrs. G. Howard Hall, Luncheon Co-chairmen; Dr. Glenn W. Toomey, President-elect, North Dakota

State Medical Association; and Mrs. Willard C. Scrivner, North Central Regional Vice-President, Woman's Auxiliary to the American Medical Association, East St. Louis, Illinois.

Dr. Toomey spoke briefly mentioning the age of the auxiliary and its accomplishments, such as the Student Loan Fund. He stressed that we auxiliary members have an opportunity to preach our medical gospel at coffee parties, P.T.A., church and other community groups.

He stated his opportunity to hear three little old ladies who were asked and refused Medicare help. They saw no point to it or the long distance phone call concerning this type of care.

In conclusion he said—"Let's not substitute anything for this gospel of our independence. Young men are needed in medicine and will not enter with socialized medicine."

The Auxiliary Past Presidents who were present were recognized. They were Betty Van der Linde, Marjorie Kermott, Ann McLean, Flo Hankins, Ruth Fischer, Audrey Mahoney and Gladys Arneson.

During the luncheon a style and wig show were presented. Door prizes and centerpieces were drawn by Mrs. Christoferson and Mrs. G. U. Ivers.

Mrs. Hieb introduced Mrs. W. Scrivner, National Regional Vice President from East St. Louis. She reminded us that we medical wives should become so well informed about our community problems and resources that we automatically become opinion makers—"not opinionated."

In discussing auxiliary maturity she stressed to increase our membersip not only numerically but by developing the potential of each individual member. She congratulated us because we have nearly one hundred percent membership. It is a privilege to belong to the woman's auxiliary as we are ambassadors—whether we wish to be or not. The type is entirely up to the individual wife.

She invited everyone to the National Convention in Chicago in June. In closing, Mrs. Scrivner thanked North Dakota for its genuine hospitality.

Mrs. Hieb dismissed the luncheon.

Mrs. R. J. Ulmer, *Recording Secretary*

Progress Report—1965-66

In our twentieth year as the Woman's Auxiliary to the North Dakota State Medical Association we have made progress:

Our membership has increased to its highest point. However, there is still a gap of ninety-two (92) to equal the membership of the North Dakota State Medical Association.

Each District has held four meetings for the year. For the most part these are health oriented, as requested by National.

We have been saddened by the departures of Mrs. Paul Burton, Mrs. Reinhold Goehl and Mrs. Robert McFadden. Their inspiration and service to this organization will influence us to greater dedication.

Your fund raising projects, memorials and donations have increased our gifts to the Medical Auxiliary Student Loan Fund and A.M.A.E.R.F. Auxiliary Fund.

A delegate from the Grand Forks Chapter of Woman's Auxiliary to Student American Medical Association has been given financial assistance to attend their National Convention in Los Angeles.

The Auxiliary members who work with Health Careers Clubs, Future Nurse Organizations and Candy Stripers surely have the satisfaction of knowing their help is appreciated and their influence will continue into the futures of all these young people.

The awareness of Mental Health progress, legislation and plans, as well as schools for the mentally retarded should help bring about changes for the better life in our State for persons in need of help.

The International Health Activities help you to clear out your closets, drawers, and husband's offices as you search for drug samples, soap, yarn, bandages and hospital gowns.

The promotion of Safety Legislation is necessary for the well being of our citizens. Surely ten ambulance accidents in one year are appalling.

Your participation in Community Service has brought about successful Blood Banks, immunizations, rehabilitation work, Disaster Nursing, Fund Drives, religious groups and numerous community organizations. Each is enriched by her assistance to others.

Mrs. E. O. Hieb, my successor, with all her ability and enthusiasm, will prove to be a most capable coordinator and presiding officer of this Auxiliary.

The work of the officers, chairmen, committee members and members in furthering the purposes of this Auxiliary has contributed to our progress.

I thank each of you for your help.

Mrs. M. A. K. Lommen, *President*

Membership Report—1965-66

A "team membership" plan was presented to the House of Delegates of the North Dakota State Medical Association in Convention in Grand Forks, North Dakota on May 2, 1965, by Mrs. Clyde Smith. They responded by recommending that their district members be billed for the Auxiliary State and National dues. With this great hope that North Dakota would join the one hundred per centers we started our year.

A letter was mailed on October 6, 1965 to the wife of each of the forty new licentiates in the state. It became evident, but not until the new fiscal year began for the State Medical Association, that most of the districts did not accept the "team membership" plan. Not until this time was it realized that after discussion in the Council, they recommended to the individual district treasurer that a composite bill be itemized and the treasurer could implement this at their own discretion. Third District collected the State and National dues and Seventh District not only paid the dues, but included a fifteen dollar contribution to the Student Loan Fund and A.M.A.E.R.F.

Last year's membership in the North Dakota Medical Association was 455. This year, as of April 4, 1966, it is 453. Last year our State Auxiliary membership was 315. This year it is 346. We have gained 31 members. This makes our comparative membership 76.3%, a relative gain of 7.1%.

We have nine organized auxiliaries and one District with seven members at large.

Perhaps the team membership plan will gain further acceptance this year. We have an obligation as a member to remind those eligible in our own districts that "the auxiliary has much to offer every physician's wife and every member has something to contribute to their community."

To belong to this auxiliary is a privilege which comes only to the wife of a physician.

Mrs. Edwin O. Hieb, *Chairman*

WASAMA Report—1965-66

The officers for the University of North Dakota chapter of WASAMA for the 1965-66 term were: Geri Kalder, President; Charlene Bratt, Vice-President; Patricia Halverson, Secretary; and Patricia Rosen, Treasurer.

The new officers began their duties April 20, 1965. The first projects were a humorous hat show for the WAAMA group, a dinner for our outgoing officers and members, and a final going away party for all WASAMA members and their husbands.

Last fall with the beginning of the academic year WASAMA started their activities by giving a welcoming tea for the new members. Each new member came with her assigned big sis and received a welcome pack, containing information about our group, the University, and about Grand Forks.

Other programs for the year included speakers: Dr. Harwood—What to Expect at Medical School and a tour of the Medical School; Mr. Robert Vallor—Malpractice suits; Mr. Donald Pearce—An Account of the Chester Fritz Collection; Dr. McLaughlin—Role of the Doctor's Wife; Mr. Rosevear and Dr. Powers—American Medical Political Action Committee; Mr. Philip Hisey—Contemporary Opera.

We saw the movie: "The Making of a Doctor." NSP demonstrated holiday cooking and gave us many ideas for Christmas gifts and decorations. In December we had a Christmas Party for all the children in our group. The freshmen wives gave a style show to the WAAMA and to the WASAMA group. One of our last programs for the year will be a makeup demonstration by a Merle Norman representative.

Our fund raising projects for the year have been a car wash, a Christmas bake sale, a dinner-dance and an Easter bazaar and bake sale. Before the year comes to a close we may have another car wash and a rummage sale. We hope to have enough funds to send one member to the national convention, which will be held in Los Angeles.

Our service projects this year are concentrated in two areas. We have been collecting old jewelry, ties, clothes, and other things for the state hospital at Jamestown. We also hope to help a member of our own group. We will spend $50.00 for a book scholarship for a married, deserving, needy, second year student. We hope this will become an annual scholarship.

We would like to thank the local WAAMA group for the support they have given us and for having us meet in their homes. We sincerely appreciate it.

The W.A.N.D.S.M.A. contributed $100.00 to assist their delegate to Convention.

Mrs. T. H. Harwood, *Liaison to W.A.S.A.M.A.*

Historian's Report—1964-65

The 41st Annual Convention of the Woman's Auxiliary to the American Medical Association was held in the St. Francis Hotel, San Francisco, California, June 21-25, 1964. Mrs. R. D. Schoregge was state delegate, Mrs. Joseph D. Craven, alternate delegate, and Mrs. Clyde Smith was presidential delegate. Mrs. Smith's report of convention was published in the October 1964 issue of *News, Views and Cues*.

Mrs. C. L. Smith, president, and Mrs. M. A. K. Lommen, President-Elect, attended the Annual Fall Conference in Chicago, October 1964. Mrs. Lommen's report appears in the October 1964 issue of *News, Views and Cues*. Mrs. E. O. Hieb, A.M.A.E.R.F. Chairman, attended the Chicago A.M.A.E.R.F. Workship on October 3, 1964. Her report appears in the February 1965 issue of *News, Views and Cues*.

The Annual Fall Board Meeting was held in the Petroleum Room of the Prince Hotel in Bismarck, November 7, 1964, with Mrs. C. L. Smith, State President, presiding, and 23 members present. The meeting was called to order at 10:30 A.M., recessed for luncheon, and was adjourned at 4:15 P.M.

The 19th Annual Meeting of the Woman's Auxiliary to the North Dakota State Medical Association was held in the new Grand Forks Country Club on May 3, 1965 with Mrs. Clyde L. Smith, State President, presiding.

Honored guest speakers at the State Convention were Dr. G. Alfred Dodds, President, North Dakota State Medical Association; Dr. Joseph D. Craven, President-Elect, North Dakota State Medical Association; and Mrs. Virgil Rae Forester, National Safety Chairman, Woman's Auxiliary to the American Medical Association, from Oklahoma City.

Official minutes are recorded in the November 1965 issue of *The Journal-Lancet*. The convention program, minutes and reports are filed in the archives.

Jacqueline Evans, *Historian*

Annual Report AMAERF—1965-66

We are going up in our contributions to A.M.A.E.R.F. But we have not reached that peak of $5.00 per capita. Congratulations to those Districts that have exceeded that amount.

Sixth District, Bismarck, had a rummage sale as a Fund Raising Project. First District, Fargo, had a benefit Ball and a Silent Auction for Fund Raising Projects.

Other contributions have been by assessment, playing cards, note paper, Christmas cards, memorials and appreciation gifts.

One kind M.D. and his wife contributed $50.00 through the Auxiliary.

Total contributions from the State: $1,492.90. Per Capita contribution: $4.32.

District	*Number of Members*	*Total Amount*	*Per Capita*
1st	82	$ 362.00	$4.41
2nd	19	33.00	1.73
3rd	54	245.00	4.53
4th	40	140.00	3.51
5th	7	——	——
6th	56	305.40	5.45
7th	29	152.50	5.29
8th	20	100.00	5.00
9th	27	85.00	3.14
10th	11	70.00	6.36
		$1,492.90	

$1,442.90 was designated to the University of North Dakota Medical School. $50.00 was designated elsewhere.

AWARDS

1. Largest contribution—First District—Fargo.
2. Largest Per Capita contribution—Tenth District—Traill-Steele
3. Greatest increase over last year—Third District—Grand Forks.

Mrs. George U. Ivers, *Chairman*

Health Careers Report—1965-66

Fargo (District 1)

Reprints of a Health Careers article printed in the Reader's Digest were ordered and delivered with pamphlets and other materials to the High School Counselors. About 30 different pieces of literature on various health careers were provided for the National Honor Society's State Convention in Fargo, March 18, 19, 1965.

Devil's Lake (District 2)

Reported no Health Careers activity due to membership scattered over wide area.

Grand Forks (District 3).

No report.

Minot (District 4)

The 6th Annual State Careers Rally was held in Minot on Sept. 18, 1965 with a representation of 117 members and 6 advisors present from Richardton, Mott, Dickinson, Minot, Mandan, Bismarck and Jamestown. The program included a tour through the Minot State College Speech and Hearing Clinic, Trinity Hospital and St. Joseph's Isotope and Psyche Depts.

Valley City (District 5)

No organized auxiliary.

Bismarck-Mandan (District 6)

Specialists lectured to the active Bismarck Medical Careers Club of 20-25 members which also included tours of both local hospitals. Many of the club members worked as Candy Stripers. They sponsored a bake sale before Christmas, netting $55.00, to provide transportation to the next State Rally with future plans for a hotdog sale. Candy Striper Dolls were made from clothespins and used as tray favors for the Pediatrics Department. The State Health Careers Chairman, with the co-operation of the Medical Careers Club and a Medical Librarian, presented a skit dramatizing the history and purpose of their club to her local Medical Auxiliary. She was also present at the Chicago Fall Conference last October. The Mandan Club, numbering 40 members, held a Quilt Sale for transportation money to the Rally and they have spent many hours as Candy Stripers. Both cities have a pin and cap awarding ceremony in May with a tea sponsored by the Auxiliary members. The Mandan group will also be holding a Pancake Supper this month.

Jamestown (District 7)

They have a Health Careers club formed, but have no current report.

Williston (District 8)

Due to a scarcity of members they report no program.

Southwest (District 9)

The Auxiliary made a $50.00 contribution to the Dickinson Future Nurses for their Scholarship Fund. Two auxiliary members are advisors to Future Nurses' Clubs in Dickinson and Richardton, with another auxiliary member advisor to the Medicorps of Mott. The latter is also vice-president of the N. Dak. Health Careers Council and was a recent representative at their National meeting in St. Louis.

Traille-Steele (District 10)

They pursue no special projects because of their small and scattered membership.

Mrs. Paul Klosterman, *Chairman*

By-Laws Report

The following changes in the By-Laws of the Woman's Auxiliary to the N.D.S.M.A. are recommended. It is also the opinion of the chairman that a supply of copies of the State By-Laws be obtained so that each District may have use of it.

RECOMMENDED CHANGES IN BY-LAWS

ARTICLE VIII—APPOINTIVE OFFICERS:

Section 1 to read: (addition of last office): The Appointive Officers of this Auxiliary shall be Corresponding Secretary, Editor, Co-Editor, and Business and Circulation Manager of Official Publications, Historian, Parliamentarian, and Liaison to Woman's Auxiliary to S.A.M.A.

Section 2 to read: (addition of part 7): (7) The Liaison to WASAMA shall acquaint herself with By-Laws of WASAMA, act as advisor to N.D. Auxiliary or Auxiliaries, and shall report in writing to the Annual Meeting of this Auxiliary on the activities of WASAMA in North Dakota.

ARTICLE IX—BOARD OF DIRECTORS

Section 1 to read: (addition of last member): The Board of Directors shall consist of officers enumerated in Article VII, Section 1 of these By-Laws, Chairmen of Standing Committees, the Immediate Past State President, President of each Component Auxiliary, the Editor, Co-Editor, and Business and Circulation Manager of our Official Publication, Corresponding Secretary, Historian, Parliamentarian, and Liaison to WASAMA.

Mrs. Paul Ahlness, *Chairman*

State Mental Health Report—1965-66

As Mental Health Chairman this year, action has been slow. Even though all the Districts have not had large programs, most have had some kind of program.

Many of our members have been extremely involved in working on some of the various committees and Task Forces within our State.

Sixth District had as one of our programs a panel on Community Mental Health Centers and gave moral support to the establishing of a Center in Bismarck, due to open in July.

Each of us, I am certain, have been involved as individuals in some phase of Mental Health work.

I have prepared a packet for each District for the coming year. Would each of the Presidents see to it that your packet is delivered to your Mental Health Chairman?

I feel we need closer contact with our District Chairmen and I hope these packets may serve as a beginning to this.

Mrs. S. J. Thakor, *Chairman*

Legislative Report—1965-66

This year of 1965-66 has not been one of great legislative activity. However, all activity in the House and Senate, both national and state were carefully watched and followed for anything of interest to us, as a medical group.

Mrs. John Van Prohaska, the regional national legislation chairman, was contacted as to what direction to take after the Medicare passage and her response was one of "watch and wait" also stating things were still a bit confused and would be for a while.

Her last letter stressed knowing our legislators on all three levels of government and to keep a file of auxiliary members who know these men for future use.

Legislation was given as a program topic in District 111 by Mrs. Chris Christu. All material available was forwarded to Mrs. Christu by me at the time.

After this period of quiet, the fall election will probably create new interest and work for the legislation committee.

Mrs. William P. Keig, *Chairman*

International Health Activities Report

All Districts participated by bringing their contributions of drugs, medical supplies, soap, bandages, and hospital gowns to Convention. Twenty-eight (28) cartons weighing seven hundred forty-seven pounds (747) were shipped to World Medical Relief, Detroit, Michigan. Shipping charges were $36.83.

Mrs. Neill F. Goltz, *Chairman*

Safety Committee Report

The Safety Committee report is, again I fear, not very successful.

A letter went out to each district urging the safety chairman to have a publicity program on Safety during the week of Jan. 24-30th, and to make a state-wide effort during this week to put Auxiliary emphasis on Safety!

One district, Sixth of Bismarck, followed this suggestion. Members of the Sixth District began a comprehensive study of the emergency services in the 11½ county area of the Bismarck District. Meeting with them were representatives of the State Health Department, and members of the fire and police departments. It was emphasized that there is a need for standards to be set regarding ambulance equipment, drivers and attendants. With the rash of accidents involving ambulances, this would seem to be a worthy project for the sixth district to pursue, and I wish to congratulate them on their choice.

My recommendation for the following year would be to work with the Medical Society, and find their wishes regarding the committees we are working to promote. We are an auxiliary to the medical society, once we find what is to be done to aid them we should go out and act.

The American Medical Association is spending several millions of dollars on public relations to improve the image of doctors in the public eye. In this way we could truly be an auxiliary to the medical society and serve the communities we live in as well. We need to let the public know we care about preventative medicine as well as curative.

Mrs. Kenneth Amstutz, *Chairman*

State Publicity Report

In March a questionnaire was sent to each district Publicity Chairman requesting information on the various forms of publicity she was able to obtain during 1965-66.

Of the 10 districts contacted, 6 responded. Half of the responding districts received as much publicity as they requested, the others seemed to require little due to inactive auxiliaries except for reporting to the newsletter. The members of inactive auxiliaries are active as individuals in their communities.

Most state newspapers have published the news of regular district meetings and rated the coverage good. Also special projects have received coverage; for example, third district's volunteer work at the Rehabilitation Center, and first district's Medical Ball.

The State newspapers will receive publicity this month on the State Convention to be held in Fargo, April 29th and 30th.

Doris Fercho, *Chairman*

Community Service Report

Our National Chairman, Mrs. Howard G. Ellis defined community service as "woman's concern toward any program or project to do with the well being of the community." She feels we should know our community, be known, interpret and publicize a conscientious program of health and to utilize our knowledge. Mrs. Ellis also points out that "No one can do everything—Everyone can do something. Above all we must care deeply."

Of the nine Districts in North Dakota there are six Community Service Chairmen. Five have reported. No report from Grand Forks, probably due to the severe flood in that area. The members assisted flood workers and provided sandwiches and coffee.

The members of the District Auxiliaries cooperated with other agencies whenever the need became evident. They worked individually or collectively in the following:

1. Parties for Senior Citizens.
2. Sponsored Health Career programs.
3. Immunization clinics and school health.
4. Mental Health programs.
5. Red Cross Blood Bank. This project under the leadership of Mrs. Don Skjei and Mrs. Allen Johnson cooperated with the Red Cross Blood Bank of Great Falls, Montana. Their group worked with ten M.D.'s every three months and collected some 211 pints of blood in the Williston area.

Individually the active, dedicated women of the Auxiliary have participated in preparation of medical supplies for foreign missions, Red Cross Disaster Nursing, United Fund, Hospital Auxiliary, Cancer Fund, Heart Fund, Board of Directors of Mary College, Ancilla Club, AAUW, Study Club, Music Club, Clothing Drives, Religious Groups, Current Events Club, Jr. Federated Women's Club, League of Women Voters, Community Theater, Welcome Wagon, National Music Week, Rainbow Girls, Scouting, P.E.O., and P.T.A.

Our members are a credit to the Auxiliary. They have done much to further good public relations as well as to create a good image of the Doctor's wife.

Mrs. Russell O. Saxvik, *Chairman*

News, Views and Cues—Managing Editor

The following is submitted as the 1966 *News, Views and Cues* Report:

We have published two issues of *News, Views and Cues* this year and plan to publish a summer issue.

We have tried to include articles by committee chairmen as well as reports of the usual district news and occasional national reports.

Again, Blue Shield has kindly paid for our postage.

I wish to thank my district news editor, Mrs. John E. Ruud, and my business manager, Mrs. John A. Lambie. Each has done a fine job.

Mrs. James R. Olson, *Managing Editor*

News, Views and Cues—District News Editor

For all Auxiliary members, *News, Views and Cues* is a means of communication between ten districts. In addition, information on national and state news, the president's reports, committee reports and all of the activities within each Auxiliary are an integral part of each issue.

Copies of your Auxiliary paper were issued in January and April, the latter issue of which was larger in size and content than the usual publications, since materials arrived to your editors too late for our scheduled February issue. We are appreciative to those districts that contributed but we are sorry that not all of the ten districts were represented.

This year we followed our outline in eight broad sections: Meetings and Auxiliary Projects, Membership, Community Service, Progeny, Illnesses, in Memoriam, Travelogue, and Miscellany.

To summarize the material in our publication this year the following is offered: The auxiliaries had interesting and worthwhile projects which generally were correlated to community service. We welcomed thirteen new members and the ten babies born to our members. We tried to acknowledge outstanding achievements of our members and their children. Our thoughts went out to those who lost a dear one.

We give our sincere thanks to councilors and their reporters and, most important, to our newsy members. We appreciate your interest and will continue to set our goals for more worthwhile and interesting issues.

Mrs. John Ruud, *District News Editor*

News, Views and Cues—Business and Circulation

All bills for publication are paid to Quality Printing Company, 111 South Fourth Street, Grand Forks, N.D.

On January 7, 1966 a total of 535 copies of *News, Views and Cues* were sent to all state Auxiliary members. A bill of $79.86 was submitted to our state treasurer and was paid.

On April 20, 1966 a total of 535 copies of *News, Views and Cues* were sent to all state Auxiliary members. This bill has not yet been received.

The third issue of the publication will be issued following the state convention in Fargo.

Copies of our publication have also been sent to the editors of state publications in each of the 50 states as well as to the AMA office in Chicago and several national officers.

Postage for the mailing of this publication is paid by Blue Shield.

Doris E. Lambie, *Business & Circulation Manager*

Budget—1966-67

Balance on hand in checking account, April 30, 1966	$1,040.64	
Bank Certificate	1,000.00	
		$2,040.64
Assumed Income—		
Dues—based on 344 members	1,032.00	$1,032.00
		$3,072.64
President's Fund:		
National Convention	$ 250.00	
Chicago Conference	125.00	
Expense Fund	125.00	
		$ 500.00
President-elect's Fund:		
Chicago Conference	$ 125.00	$ 125.00
Other Funds:		
Committee Chairman	$ 60.00	
News, Views and Cues	250.00	
Past President's Pin	9.00	
A.M.A.E.R.F.	25.00	
W.A.S.A.M.A.	100.00	
Miscellaneous Fund	50.00	
Postage for I.H.A. (Samples, etc.)	50.00	
		$ 544.00
Total Expense Funds		$1,169.00

Finance Committee
Margaret Hanewald, *Chairman*

Financial Statement

May 1, 1965—April 30, 1966

May 1, 1965 Balance on Hand	$ 833.25	
Dues:		
344 National	1,709.00	
9 Past Dues 1964-1965	36.00	
Bank Certificate Int. 6/30/65-3/31/66	71.25	
Past President Pin	9.76	
		$2,659.24
Disbursements:		
Mrs. M. A. K. Lommen, President:		
National Convention 1965	250.00	
Chicago Conference 1965	125.00	
Mrs. E. O. Hieb, President-Elect:		
Chicago Conference 1965	125.00	
National Treasurer (Includes Mrs. Artz)	697.00	
Miscellaneous Fund:		
Mrs. E. Hieb (Postage)	12.77	
Mrs. C. Fercho (Medicine Postage)	40.27	
Mrs. R. Hankins (Postage, Telephone)	24.84	
Mrs. R. Tudor (Telephone)	4.73	
Mrs. James Moses (Postage)	5.52	
News, Views, and Cues	212.02	
North Dakota Council—Health Careers	5.00	
W.A.S.A.M.A.—Mrs. T. H. Harwood	100.00	
Past President Pin	16.45	
		$1,618.60
April 30, 1966 Balance on Hand		$1,040.64
Bank Certificate—		
Dakota National Bank—Bismarck		$1,000.00

Number of Members—1965-66

District	*Total*	*New Members*	*Deceased*
1	80 State		
	82 Nat'l.	8	1 Mrs. Paul Burton
2	19	3	
3	54	11	1 Mrs. R. O. Goehl
4	40	4	
5	7	7	
6	56	8	
7	28	8	
8	20	4	
9	27	1	
10	11	1	
	344 Nat'l.	55	
	342 State		

1964-65

1	78
2	24
3	46
4	40
5	—
6	53
7	22
8	13
9	23
10	11
	310

Auxiliary Convention Report—1966

DEPOSITS:		
From Lyle Limond	$ 200.00	
Registration and luncheon tickets	372.00	
		$ 572.00
EXPENSES:		
Bank charge for checking account	$ 2.50	
Town House—for luncheon	307.23	
Fargo Music Club—rental of decorations	3.50	
Sally Wold—luncheon expenses	3.50	
Ruth Hall—luncheon expenses	5.50	
Eve Lane—registration supplies	3.50	
Martinson's—gift	10.00	
McShane's—gifts	31.49	
Shotwell Floral	95.62	
Leeby's—fruit baskets	7.16	
Town House—coffee hour	4.50	
Total Expenses		$ 474.50
Balance		$ 97.50

A check for the balance remaining of $97.50 was sent to Lyle Limond. $97.50 check forwarded to Mrs. Roger Berg 6/1/66.

Jeanne Houghton, *Finance Chairman*

Medical Auxiliary Student Loan Fund Report

Our Student Loan Fund has operated successfully for 16 years. At the State Convention last May in Grand Forks, Dean Harwood and Assistant Dean Arnason approved the recommendation to send all Student Loan Fund money to A.M.A.E.R.F., designated to the University of North Dakota Medical School. At that meeting it was also recommended that each District give $10.00 per member to Student Loan. Some Districts have fallen short of this. It is my sincere hope that next year they will do better.

In a recent letter from Dean Arnason, he reported that 29 loans were made in sums ranging from $125.00 to $600.00. All except three were in the $300 to $500 range.

District Reports

1st District, Fargo	84 members	$550.00
2nd District, Devils Lake	19 members	30.00
3rd District, Grand Forks	54 members	570.00
4th District, Minot	40 members	400.00
5th District at Large Valley City	7 members	
6th District, Bismarck	56 members	560.00
7th District, Jamestown	28 members	280.00
8th District, Williston	20 members	15.00
9th District, Dickinson	27 members	75.00
10th District, Traill-Steele	11 members	20.00

Memorials: Gifts:

E. J. Buckingham—Capital City Clinic	100.00
E. J. Buckingham—R. E. Hankins, M.D.	10.00
Mrs. John Moses—R. E. Hankins, M.D.	10.00
Lee Christoferson, M.D.	25.00
	$2,645.00

Mrs. M. H. Poindexter, *Chairman*

Medical Auxiliary Loan Fund Report

NET WORTH:			
Notes Receivable		$32,717.62	
Cash (Deficit)		617.17	
TOTAL			$32,100.45
EXPENDITURE REPORT:			
Cash Balance, January 1, 1965			$ 2,476.24
Receipts: New Funds			
Lee Christoferson	$ 25.00		
Med. Auxiliary	2,577.00		
R. E. Hankins	20.00		
Capital City Clinic	100.00		
		$ 2,722.00	
Principal		$ 6,304.38	
Interest		265.21	
			$ 9,291.59
Total Receipts			11,767.83
Less Expenditures			12,385.00
Deficit Cash Balance, Dec. 31, 1965			—$ 617.17

A total of 29 loans were made in sums ranging from $125 to $600. All except three were in the $300 to $500 range.

Report of the Nominating Committee

Proposed slate of Officers for 1966-67.

President, Mrs. E. O. Hieb (Pat), Seventh District

President-Elect, Mrs. L. G. Pray (Helen), First District

First Vice-President, Mrs. H. W. Evans (Jacque), Third District

Second Vice-President, Mrs. Carl B. London (Virginia), Fourth District

Recording Secretary, Mrs. P. Ahlness (Peg), Ninth District

Treasurer, Mrs. R. M. Berg (Florence), Sixth District.

Mrs. C. L. Smith, *Chairman*

Auxiliary President's Report—First District

We have 82 members this year. Death has claimed another one of our beloved members, Mrs. Paul Burton. We have missed her.

We have enjoyed good attendance at our four luncheon meetings. Programs have been varied, informative and most interesting.

Mrs. Calvin Fercho talked and showed slides of their two month stay in Haiti. Dr. and Mrs. Fercho were there through FOCUS, Inc. as a Medical Doctor and assistant.

Our State President, Mrs. M. A. K. Lommen, was our honored guest at our November meeting. She brought us up to date on the fall workshop in Chicago and the Fall Board Meeting in Bismarck.

Mrs. Chris Christu spoke to us regarding legislation at our January meeting.

Mrs. Christu was mentioned as one of the outstanding Women of America this past year.

Dr. R. C. Bushland, Entomologist at N.D.S.U., spoke to us on the topic, "Advanced Research in Insecticide Residue," at our March meeting.

We had a Medical Ball on February 19 at the F.M. Hotel, with "Mid-winter's Nights Dream," as the theme. Mrs. Robert Ivers and Mrs. Matt Ehlen were Co-Chairmen. Committee Chairmen and all did an excellent job. All reports were favorable and the Auxiliary has voted to have another Medical Ball next year.

On Friday, April 22, we enjoyed an extra day together.

A "Spring Fling," which was a luncheon at the newly remodeled and redecorated Fargo Country Club. It was intended to be a *strictly for fun* affair with a silent auction to help boost our contributions to the Student Loan and A.M.A.E.R.F.

Our District Contribution to Student Loan is $550.00. District contribution to A.M.A.E.R.F. is $250.00. We have $112.00 in addition to this in memorials and one appreciation gift. Total contributions $912.00.

New officers for 1966-67 will be: Mrs. L. G. Pray, President; Mrs. J. B. Wenzel, Vice-President; Mrs. D. C. Kana, Secretary; Mrs. Frank Melton, Treasurer; Mrs. Donald Barnard, Councilor.

Our auxiliary continues to provide cakes for the Y.W.C.A. Senior Citizens bi-monthly.

Doctor's wives serve in so many ways and in so many organizations that it is difficult to enumerate them.

My two years as President of First District have been most rewarding and enjoyable. I would like to take this opportunity to say thank you to each and every one of you for making it so.

Mrs. George U. Ivers, *President*

Auxiliary President's Report—Second District

The Second District Medical Auxiliary held four business meetings during the past year. Mrs. John Beck gave a demonstration on the making of ceramics at our October meeting. Mr. A. L. Haroldson, Mental Health chairman, explained to us what is being done regarding the proposed Mental Health Clinics in our area in December. A movie was shown at our February meeting and Mrs. M. A. K. Lommen, State President, visited our district in April. New officers were elected at this meeting. They are Mrs. Robert Miller, Bottineau, president; Mrs. David Rinn, Cando, Secretary-Treasurer; Mrs. Jerry Terlecki, Minnewaukan, Councilor. Mrs. William Turkula, Devils Lake, was chosen Delegate to the State Convention in Fargo, April 29-30.

Two of our members are on state committees. Mrs. Jon Eylands is on the Student Loan Fund Committee and Mrs. Donald McIntyre is on the Nominations Committee. Our members are also active in various local organizations such as P.T.A., Hospital Auxiliaries, Red Cross, and church groups.

There are 19 members in Second District. $23.00 was contributed to AMERF and $30.00 to Student Loan Fund.

Mrs. Ernest Gilbertson, *President*

Auxiliary President's Report—Third District

The Grand Forks Auxiliary to the Third District Medical Society has fifty-three (53) members in good standing.

We held four meetings during the 1965-66 year. Our first meeting was a dessert luncheon held at the home of Mrs. Rodney Clark on October 21. Mrs. Sadie Fitts, director of the Valley Day Care Center, spoke to us on the problems and rewards of teaching uneducable, but trainable retarded children. Mrs. Edna Sandmeyer read a moving memoriam to Mrs. Reinhold O. Goehl who died in August 1965.

The second meeting was a dinner meeting held November 18 at the Golden Hour. Our State President, Mrs. M. A. K. Lommen, was our guest speaker giving an informative and interesting talk on Auxiliary projects and goals.

Our third meeting was a dinner meeting at the Golden Hour on January 20. Our speaker was Mr. Norbert Auer who gave an eye-opening and informative talk on Urban Renewal.

Our last meeting was held March 17 at the home of Mrs. Harold Evans. Speaking to us was Mr. Philip Hisey from the University who spoke on modern opera. Annual Reports were given and new officers were elected.

Our Auxiliary as a group, has been very active in community service this year. Tuesday is our day for volunteer service at the University Rehabilitation Center. For the Valley Day Care Center we pay the tuition for one child and also do secretarial work for Mrs. Fitts. During the flood emergency our group spent many days working in the Red Cross kitchen and on mobile units.

Our AMA/ERF donations as of April 12, 1966 were $245. A great increase over past years.

Our Student Loan Fund Benefit Dance was held on April 2, 1966 at the Westward Ho. Our contribution to the fund was approximately $570.

Collecting our dues through the men was extremely difficult and as many of the doctors do not pay their dues until March or April, our dues were quite late.

This has been a very rewarding year for me and every member has been most co-operative.

The following officers were elected for 1966-67:

President, Mrs. Ralph Mahowald; Vice-President, Mrs. George Wilson; Secretary, Mrs. John Lambie; Treasurer, Mrs. Douglas Doss; Councilor, Mrs. John Ruud; Convention Delegates, Mrs. Harold W. Evans and Mrs. Ralph Mahowald.

Mrs. Thomas L. Schafer, *President*

Auxiliary President's Report—Fourth District

Membership in the Northwest District consists of forty members. There were four meetings held during the year. The first was a luncheon held at the Embers Restaurant on October 18th. The theme was "Getting to Know You" and a general business meeting was held.

The doctors' wives at the Air Force Base were hostesses for our second meeting, which was held at their Officers Club in November. Following the business meeting, a demonstration and talk about painting china was given.

On February 25th, we met at the Clarence Parker Hotel for lunch and a discussion on wigs, wiglets and hair pieces. Our final meeting was a dinner meeting at the Riverside Restaurant. Mrs. Lommen, our State Auxiliary President, was our guest. She reported on the year's activities of the Auxiliary and other matters of interest to us.

Our District supported the Student Loan Fund with a donation of $400. We gave $140 to the A.M.A.E.R.F. A local institution to which we contributed $50 is The Exceptional Children's School. This money was from the treasury; we had no money-making projects during the year.

Our officers for the coming year are: President, Mrs. William Hurley; Vice-President, Mrs. Fred A. Veenbaas; Secretary, Mrs. George Hart; Treasurer, Mrs. Jens Sahl; Councilor, Mrs. Samuel Shea.

Our delegates to the convention are Mrs. V. J. Fischer and Mrs. W. B. Huntley.

The Fourth District members on the State Board this year are: Fourth District President, Mrs. M. W. Garrison; Fourth District Councilor, Mrs. Samuel Shea; Safety Chairman, Mrs. Kenneth Amstutz; Member of Student Loan Fund Committee, Mrs. Paul Breslich; Member of

Nomination Committee, Mrs. V. J. Fischer; and alternate member of Nominating Committee, Mrs. L. H. Kermott.

Mrs. M. W. Garrison, *President*

Auxiliary President's Report—Sixth District

During the 1965-66 year, the Sixth District Medical Auxiliary held four meetings. Two were dinner meetings and two were luncheons.

Our first meeting was held on September 25 in conjunction with the men. We also were guests for the program which was on Cancer Quackery with a lawyer from A.M.A. Headquarters giving us the inside story. It was surely startling to find the vast amount of money involved in these transactions.

Our Rummage Sale for AMAERF was held on October 23 and netted us $177. It was under the able guidance of our AMAERF Chairman, Mrs. Bill Buckingham, assisted by Mrs. James Moses.

The November luncheon proved to be not only enjoyable but also educational. A panel consisting of Mrs. R. W. Wheeler, Mrs. Phil Teigen and Father Arnold Spain explained new Mental Health Legislation and Implementation. Afterwards the group voted to give moral support to the establishment of a Mental Health and Retardation Center in Bismarck.

December again reminded us of those who are less fortunate than we and we sent $15 to Open Your Heart, Community Christmas Fund.

January found us again out but purely for a social evening as guests of Sixth District. No formal meeting was held.

February 22 found us back at our "homestead," the Prince Hotel for a lovely dinner meeting. The attendance was good and the program excellent. Mrs. Paul Klosterman was program chairman and presented her subject, Health Careers, very creatively. She had her Medical Career Club members present a skit, written by Mrs. Barbara Cowles, local Medical Record Librarian, dealing with the history of the Bismarck Club. Later a series of slides from A.M.A. dealing with Health Careers was shown. We should all be very proud of the group we sponsor.

We also voted at this meeting to assist with a proposed "Pap Smear Clinic," to be held in Bismarck when all details are worked out.

Our last meeting was held at the home of Iris Schoregge on March 22. A Foreign Flavors Luncheon with members preparing dishes of their native lands was served. A tremendous turnout of 41 members attended. We had as our guest speaker, Mrs. M. A. K. Lommen, our State President. She gave a most informative speech and stirred us to action for the Auxiliary.

May I express my thanks to all who worked so very hard on the luncheon.

New officers elected for 1966-67 were as follows:

President, Mrs. Charles Hamilton; Vice-President, Mrs. Roger Fricke; Secretary, Mrs. Al Fortman; Treasurer, Mrs. G. Gonzales; Councilor, Mrs. R. Tudor.

Delegates to the Convention: Mrs. Russell Saxvik and Mrs. Paul Klosterman.

We were pleased to have eight Board Members this year from Bismarck. Mrs. M. A. K. Lommen, State President; Mrs. Robert Tudor, Councilor; Mrs. Clyde Smith, Chairman of Nominating Committee; Mrs. Paul Klosterman, State Health Careers Chairman; Mrs. Russell Saxvik, State Community Service Chairman; Mrs. James Moses, Corresponding Secretary; Mrs. Roger Berg, Treasurer; Mrs. S. J. Thakor, State Mental Health Chairman and Sixth District President.

We had a total membership of 54.

Our contribution breakdown: AMAERF $200 (sent in June 1965 to be credited to this year) $87.50 sent in 1966, for a total of $287.50. $550 Student Loan and $15 to Christmas Fund.

I would like to extend my sincere thank-you to all the Chairmen of all my Committees for working so hard during this past year. The saying that the whole is only as good as the parts applies well here, I think.

We're Excellent!!

Mrs. S. J. Thakor, *President*

Auxiliary President's Report—Seventh District

The Seventh District Medical Auxiliary met four times for meetings, and in addition, met twice more at the invitation of the Medical Society for dinner and participation in their program. With the cooperation of the Society, we have been able to attain full 100% membership in the Auxiliary and this year our membership has risen to 28 plus our one Life Member, Mrs. Arzt. Our per member contribution to the Student Loan Fund and AMAERF was $15 and additional contributions to AMAERF were $7.50, making the total of all contributions $427.50.

We have tried to encourage the growth of the Medical Careers Club and the further involvement of the Auxiliary members. Twenty-three girls are active members, and they with two Auxiliary advisors attended the State Rally in Minot last fall. We lent chauffering service to their Christmas caroling activities. Several Auxiliary members assisted in training sessions for Candy Stripers at Jamestown Hospital in April. Our final program for Auxiliary for the year was conducted by Miss Delores Henne, advisor of the Medical Careers Club, and Miss Ellagrace Reekie, Director of Nursing at Jamestown College. A Candy Striper and a Senior nursing student at the College each also contributed to the presentation. Several Auxiliary members volunteered to drive Senior nursing students to outlying high schools for speaking engagements. The group suggested that efforts be made to enlarge the Medical Careers Club both in numbers and in scope, and that special efforts be made to establish a group for young men who may have interest in seeking careers in medicine. We shall continue efforts in these areas next year.

Our Auxiliary members actively supported our Christmas Basket project in 1965. Clothing, newly purchased gift-wrapped articles, and a generous supply of foodstuffs was delivered to two very needy families in Jamestown.

We entertained Mrs. Lommen, the State President, at our December meeting. Dr. Gerald Swafford spoke to us about Educational Television at our October meeting. In February we viewed "Maganga," a film distributed by the Warner-Chilcott Pharmaceutical Co. which shows the vast contrast between African medicine today as practiced by properly trained physicians and as still practiced in remote areas by native witch doctors.

The officers for Seventh District for 1966-67 are as follows:

President, Mrs. John Beall; Vice-President, Mrs. Gerald Swafford; Secretary-Treasurer, Mrs. James Miles; Councilor, Mrs. George Holt. Delegate to Convention, Mrs. John Beall.

Mrs. Philip Curtis, *President*

Auxiliary President's Report—Eighth District

The Kotana Medical Auxiliary of District 8 met February 12, 1965 to elect officers. The following were elected or appointed: President, Mrs. R. E. Wiederanders; Vice-President, Mrs. M. J. Olson; Secretary-Treasurer, Mrs. Gyman Okeson; Councilor, Mrs. Dean Strinden; Delegate, Mrs. J. D. Craven.

March 18 the Auxiliary met with the Kotana Society for a dinner meeting. Plans were discussed for the O.B.—Gyn meeting to be held in the fall. The following officers were elected. Legislation, Mrs. Chester Borrud; AMAERF, Mrs. Alan Johnson; Community Service, Mrs. Donald Skjei.

In September the Auxiliary sponsored a coffee reception for the wives of the O.B. conference which was held in Williston. A luncheon was also sponsored for these guests which was followed by a tour of Fort Buford and Fort Union.

In January a dinner meeting was held for election of officers. The following were elected: President, Mrs. J. D. Craven; Vice-President, Mrs. M. J. Olson; Secretary-Treasurer, Mrs. F. E. McCoy; Councilor, Mrs. Gordan Ellis; Delegate, Mrs. J. D. Craven; Community Service, Mrs. Donald Skjei; AMAERF, Mrs. Alan Johnson; Legislation, Mrs. Chester Borrud.

Every three or four months when the Williams County Blood Bank has its drive in Williston, 8 or 10 of the doctors' wives are very active in helping make the drive successful. Mrs. Alan Johnson is General Chairman for Williams County.

In March Mrs. M. A. K. Lommen, State Auxiliary President honored us with her presence at a dinner meeting.

As a group we have no special projects. Members are active or semi-active in the hospital auxiliaries of Williston. There are 20 members for the current year. Our delegate to the state convention will be Mrs. J. D. Craven.

The Eighth District contributions to the Medical Auxiliary Student Loan Fund were $15 and to AMAERF were $100.

Mrs. M. J. Olson, *Secretary-Treasurer*

Auxiliary President's Report—Ninth District

Five meetings of the Ninth District Auxiliary were held during the past year. Two were devoted to business matters and three were dinner gatherings with our husbands.

Three members of the Southwest District, Margaret Hanewald, Dickinson, Jean Slominski, Richardton, and Flo Hankins of Mott, have been working actively with our Future Nurses Organizations. Other members have aided Hospital Auxiliaries and District Nursing Homes in the area.

Fifty dollars was contributed to the Dickinson Future Nurses. A direct gift of seventy-five dollars was made to the Medical Student Loan Fund at the University of North Dakota, and an additional seventy-five dollars to the same fund through a contribution to the AMAERF.

Officers for the coming year are:

President, Mrs. Andrew C. Sawchuk, Dickinson; Vice-President, Mrs. L. H. Reichert, Dickinson; Secretary-Treasurer, Mrs. Harlan C. Larson, Dickinson; Councilor, Mrs. Walter Hanewald, Dickinson.

The Ninth District Auxiliary has twenty-seven dues-paying members in 1965-66. Delegate to the 1966 State Convention is Mrs. Robert Hankins, Mott.

Mrs. H. E. Guloien, *President*

Auxiliary President's Report—Tenth District

The Tenth District Medical Auxiliary has 11 members. We have four meetings a year. Our group does not participate in the various activities as there are few members, but we contribute to the AMAERF and Student Loan Fund.

The officers for 1966-67 are: Mrs. Ronald Kloster, Mayville, President; Mrs. Donald Breen, Hillsboro, Vice-President; Mrs. Delbert Hlavinka, Mayville, Secretary-Treasurer; Mrs. Robert McLean, Hillsboro, Councilor.

Mrs. Karl Oja, *President*

Post Convention Board Meeting

Mrs. E. O. Hieb, President, called the meeting to order in the Regency Room immediately following the Annual Meeting.

The following were elected to the Nominating Committee: Mrs. M. A. K. Lommen, Chairman, assisted by Mrs. Robert Hankins, Mrs. Calvin Fercho, Mrs. John Ruud and Mrs. George Hart. Alternates are Mrs. Charles Arneson, Mrs. Robert Schoregge, Mrs. Robert Tudor, and Mrs. Philip Dahl.

Mrs. Hieb announced that the Fall Board Meeting will be held on October 8th in Jamestown. She would prefer to visit the Districts early in the Fall before bad weather sets in.

Mrs. L. G. Pray will be the State Delegate to the AMA convention, Medical Auxiliary, in Chicago, Drake Hotel, June 26-30. Mrs. E. O. Hieb will be the Presidential Delegate. There is no alternate.

Mrs. S. J. Thakor moved the meeting adjourn. Mrs. J. Moses seconded the motion. The motion carried. The meeting was adjourned.

Mrs. R. J. Ulmer, *Recording Secretary*

Woman's Auxiliary Program

Headquarters—Town House

Friday, April 29, 1966

1:00 - 2:00 P.M.	Registration. Lobby of Town House. Chairmen: Mrs. Mark Lane, Mrs. J. W. Miller.
2:00 P.M.	Nominating Committee Meeting. Regency Room, Town House. Mrs. Clyde Smith, Chairman; Mrs. V. J. Fischer, Mrs. Paul Ahlness, Mrs. Joseph D. Craven, Mrs. Donald McIntyre.
2:30 P.M.	Finance Committee Meeting. Regency Room. Town House. Mrs. Walter C. Hanewald, Chairman: Mrs. Joseph D. Craven, Mrs. Rodney G. Clark, Mrs. Roger M. Berg, Treasurer; Mrs. Thomas E. Pederson.
3:00 P.M.	Medical Auxiliary Student Loan Fund Meeting. Regency Room, Town House. Mrs. M. H. Poindexter, Chairman; Mrs. James J. Moses; Mrs. Paul Breslich, Mrs. Jon V. Eylands; Mrs. Paul Ahlness.
3:30 P.M.	Pre-Convention Board Meeting. Regency Room. Town House.

Saturday, April 30, 1966

8:00 A.M.	Past Presidents' Breakfast. Town House, Mrs. Stephen Bacheller, Chairman.
8.30 - 9:30 A.M.	Registration. Lobby of Town House.
9:30 A.M.	Opening Session. Regency Room, Town House. Mrs. M. A. K. Lommen, State President, presiding. Pledge of Loyalty: Mrs. E. O. Hieb, State President-Elect. Invocation: Mrs. L. G. Pray, Incoming President of First District. Welcome: Mrs. G. U. Ivers, President, First District Auxiliary. Response: Mrs. Sushen J. Thakor, President, Sixth District Auxiliary. Greetings: Dr. Joseph D. Craven, President, North Dakota State Medical Association. In Memoriam: Mrs. Frank M. Melton, Mrs. J. R. Goff, Mrs. N. F. Goltz. Roll Call: Mrs. R. J. Ulmer, Recording Secretary. Reports.
12:00 Noon	Recess

12:30 P.M.	Luncheon. Embassy Room, Town House. Mrs. G. Howard Hall, Mrs. Lester E. Wold, Chairmen. Mrs. E. O. Hieb, President-Elect, presiding. Address: Dr. Glenn W. Toomey, President-Elect, North Dakota State Medical Association. Address: Mrs. Willard C. Scrivner, North Central Regional Vice-President, Woman's Auxiliary to the American Medical Association, East St. Louis, Illinois.
2:30 P.M.	Continuation of Session. Regency Room. Town House. Reports. Installation of Officers by Mrs. Willard C. Scrivner.
4:15 P.M.	Adjourn. Coffee Break.
4:30 P.M.	Post-Convention Board Meeting.
6:30 P.M.	Mixer. Upper level of Civic Memorial Auditorium.

Convention Committees

1. *Registration and Tickets*
   Mrs. Mark Lane, 521 Southwood Drive, Fargo
   Mrs. J. W. Miller, 621 Southwood Drive, Fargo
2. *Hospitality and Courtesy*
   Mrs. B. A. Mazur, 2314 6th St. South, Fargo
3. *Publicity*
   Mrs. Calvin K. Fercho, 1747 So. 7th St., Fargo
4. *Finance*
   Mrs. James Houghton, 1707 South 9th St., Fargo
5. *Past President's Dinner*
   Mrs. Stephen C. Bacheller, Enderlin
6. *Luncheon*
   Mrs. G. Howard Hall, 1748 So. 9th St., Fargo
   Mrs. Lester E. Wold, 1708 So. 9th St., Fargo
7. *Memorial Service*
   Mrs. Frank Melton, 1702 So. 7th St., Fargo
   Mrs. John R. Goff, 1441 So. 8th St., Fargo
   Mrs. Neill F. Goltz, 804 So. 8th St., Fargo
8. *I.H.A. Packing Committee*
   Mrs. Neill F. Goltz, 804 So. 8th St., Fargo
   Mrs. Calvin Fercho, 1747 So. 7th St., Fargo
   Mrs. William Kelly, 1136 No. 17th St., Fargo
   Mrs. D. H. Lawrence, 720 No. 7th St., Fargo
9. *Convention Chairman*
   Mrs. Lee Christoferson, 1307 So. 6th St., Fargo
10. *Pages*
    Mrs. Walter C. Hanewald, 1043 5th Ave. W., Dickinson
    Mrs. James J. Moses, 1111 W. Highland Acres Road, Bismarck
11. *Auditing*
    Mrs. V. J. Fischer, 303 8th Ave. S.E., Minot
    Mrs. L. H. Kermott, 200 7th Ave. S.E., Minot

1966-1967 Officers and Committee Chairmen

STATE OFFICERS:

President: Mrs. E. O. Hieb, 211 Hillcrest Dr. N.E., Jamestown.
President-Elect: Mrs. L. G. Pray, 1701 So. 8th St., Fargo.
First Vice-president: Mrs. H. W. Evans, 2624 Olson Drive, Grand Forks.
Second Vice-president: Mrs. Carl B. London, 506 Main St. So., Minot.
Recording Secretary: Mrs. Paul Ahlness, Bowman.
Treasurer: Mrs. Roger M. Berg, 219 W. Ave. B, Bismarck.
Corresponding Secretary: Mrs. G. Holt, 214 2nd Ave. S.W., Jamestown.

COMMITTEE CHAIRMEN:

Membership: Mrs. L. G. Pray, 1701 So. 8th St., Fargo.
Program: Mrs. H. W. Evans, 2624 Olson Drive, Grand Forks.
Nominating: Mrs. M. A. K. Lommen, 831 Griffin St., Bismarck.
Parliamentarian: Mrs. Clyde Smith, 622 Raymond St., Bismarck.
Liaison to W.A.S.A.M.A.: Mrs. Thomas Schafer, 1523 Cottonwood St., Grand Forks.
Historian: Mrs. Walter Hanewald, 1043 5th Avenue West, Dickinson.
A.M.A.E.R.F.: Mrs. R. D. Schoregge, 621 Avenue F West, Bismarck.
Health Careers: Mrs. P. F. Klosterman, 1529 No. 18th St., Bismarck.
By-Laws: Mrs. V. J. Fischer, 303 8th Avenue S.E., Minot.
Mental Health: Mrs. S. J. Thakor, 907 Griffin St., Bismarck.
Legislation: Mrs. Chris H. Christu, 1509 So. 5th St., Fargo.
Disaster Preparedness: Mrs. Robert McLean, Hillsboro.
International Health Activities: Mrs. James V. Miles, 722 6th Ave. S.E., Jamestown.
Publicity: Mrs. M. H. Poindexter, 1350 So. 9th St., Fargo.
Safety: Mrs. K. N. Amstutz, 412 8th Ave. S.E., Minot.
Official Publication: News, Views and Cues.
  Managing Editor: Mrs. James R. Olson, 1506 Chestnut St., Grand Forks.
  District News Editor: Mrs. R. G. Clark, 2629 Olson Dr., Grand Forks.
  Business and Circulation: Mrs. John A. Lambie, 2721 Chestnut St., Grand Forks.
Community Service: Mrs. Mack V. Traynor, 1310 South 9th St., Fargo.

SPECIAL COMMITTEES

Reading: Mrs. R. O. Saxvik, 1243 W. Highland Acres Rd., Bismarck; Mrs. R. B. Tudor, 714 Ave. C West, Bismarck.
Resolutions: Chairman to be appointed later by the Bismarck convention committee.
Nominations: Mrs. M. A. K. Lommen, 831 Griffin St., Bismarck, Chairman; Mrs. Robert Hankins, Mott; Mrs. Calvin Fercho, 1747 S. 7th St., Fargo; Mrs. John Ruud, 2221 Chestnut, Grand Forks; Mrs. George Hart, 213 7th Ave. S.E., Minot. Alternates are: Mrs. Charles Arneson, 714 Second St., Bismarck; Mrs. Robert Schoregge, 621 Ave. F West, Bismarck; Mrs. Robert Tudor, 714 Avenue C West, Bismarck; and Mrs. Philip Dahl, 1127 West Highland Acres Road, Bismarck.
Finance: Mrs. Joseph D. Craven, 915 Second Ave., Williston, Chairman; Mrs. Rodney G. Clark, 2629 Olson Drive, Grand Forks; Mrs. Roger M. Berg, 219 W. Avenue B, Bismarck; Mrs. Thomas E. Pederson, 416 4th Ave. N.E., Jamestown; and Mrs. John Beall, 421 4th Ave. S.E., Jamestown.
Medical Auxiliary Student Loan: Mrs. James J. Moses, 1111 W. Highland Acres Rd., Bismarck, Chairman; Mrs. Paul Breslich, 818 4th St. S.E., Minot; Mrs. Jon V. Eylands, 710 W. 3rd St., Rugby; Mrs. Paul Ahlness, Bowman; and Mrs. J. F. Houghton, 1707 S. 9th St., Fargo.
Nurse Loan Committee: Mrs. Clyde Smith, 622 Raymond St., Bismarck, Chairman; Mrs. J. J. Moses, 1111 W. Highland Acres Rd., Bismarck; and Mrs. M. A. K. Lommen, 831 Griffin St., Bismarck.
Delegates to National Convention, Chicago, June 26-30, 1966. Mrs. L. G. Pray, 1701 S. 8th St., State Delegate. Mrs. E. O. Hieh, 211 Hillcrest Dr. N.E., Jamestown, Presidential Delegate. Alternate: None.

DISTRICT PRESIDENTS–1966-67

First District: Mrs. L. G. Pray, 1701 So. 6th St., Fargo.
Second District: Mrs. C. R. Miller, 1207 Bennett, Bottineau.
Third District: Mrs. Ralph E. Mahowald, 606 So. 5th St., Grand Forks.
Fourth District: Mrs. William C. Hurly, 6 9th St. S.E., Minot.
Sixth District: Mrs. C. A. Hamilton, 1129 No. Parkview Dr., Bismarck.
Seventh District: Mrs. John Beall, 421 4th Ave. S.E., Jamestown.
Eighth District: Mrs. Joseph D. Craven, 915 Second Ave., Williston.
Ninth District: Mrs. Andrew C. Sawchuk, 127 8th Ave. West, Dickinson.
Tenth District: Mrs. Ronald Kloster, Mayville.

DISTRICT COUNCILORS–1966-67

First District: Mrs. Donald M. Barnard, 1212 So. 7th St., Fargo.
Second District: Mrs. J. Terlecki, Minnewaukan.
Third District: Mrs. John E. Ruud, 2221 Chestnut, Grand Forks.
Fourth District: Mrs. Samuel Shea, 808 1st St. S.E., Minot.
Sixth District: Mrs. R. B. Tudor, 714 Ave. C West, Bismarck.
Seventh District: Mrs. G. Holt, 214 2nd Ave. S.W., Jamestown.
Eighth District: Mrs. G. E. Ellis, N.E. of City, Williston.
Ninth District: Mrs. Walter C. Hanewald, 1043 5th Avenue West, Dickinson.
Tenth District: Mrs. R. W. McLean, Hillsboro.

WOMAN'S AUXILIARY TO THE NORTH DAKOTA STATE MEDICAL ASSOCIATION 1966-67 MEMBERSHIP ROSTER

First District

Amidon, Mrs. B. F.	1701 9th Street So., Fargo
Anderson, Mrs. U. Schuyler	V.A. Center, Fargo (Associate)
Bacheller, Mrs. Stephen C.	Enderlin
Barnard, Mrs. Donald M.	1212 S. 7th. Street, Fargo
Beithon, Mrs. E. J.	429 N. 5th Street, Wahpeton
Bergan, Mrs. Donald E.	V.A. Center, Fargo (Associate)
Bond, Mrs. John M.	314 Oakland Ave. S., Fargo
Borland, Mrs. V. G.	1710 8th St. So., Fargo
Bushell, Mrs. Robert	55 Woodland Drive, Fargo
Christoferson, Mrs. Lee	1307 So. 6th Street, Fargo
Christu, Mrs. Chris N.	1509 S. 5th Ave., Moorhead
Darrow, Mrs. Kent E.	716 So. 8th St., Fargo
DeCesare, Mrs. F. A.	1401 So. 9th St., Fargo
Dodds, Mrs. G. Alfred	1602 So. 10th St., Fargo
Ehlen, Mrs. Matt	94 22nd Ave. N., Fargo
Engstrom, Mrs. Perry	Wahpeton
Fercho, Mrs. Calvin K.	1747 So. 7th St., Fargo
Fjelde, Mrs. J. H.	711 Broadway, Fargo
Fortin, Mrs. H. J.	1440 So. 8th St., Fargo
Gaebe, Mrs. Robert C.	1702 So. 15th St., Moorhead
Geib, Mrs. Marvin J.	1219 So. 4th Ave., Moorhead
Geston, Mrs. Robert	701 West Elm, West Fargo
Gillam, Mrs. John S.	1433 So. 7th St., Fargo
Goff, Mrs. John R.	1441 So. 8th St., Fargo
Goltz, Mrs. Neill F.	804 So. 8th St., Fargo
Gustafson, Mrs. Maynard B.	1201 So. 8th St., Fargo
Hall, Mrs. G. Howard	1748 So. 9th St., Fargo
Halliday, Mrs. Ross	118 24th Ave. No., Fargo
Hamilton, Mrs. T. M.	River Oaks, Moorhead
Hawn, Mrs. Hugh W.	1325 No. 1st St., Fargo
Heilman, Mrs. Charles O.	49 No. 18th Ave., Fargo
Houghton, Mrs. James F.	1707 So. 9th St., Fargo
Hunter, Mrs. Cornelius M.	1434 So. 6th St., Fargo
Ivers, Mrs. George U.	1106 So. 10th St., Fargo
Ivers, Mrs. R. R.	809 So. 8th St., Fargo
Jaehning, Mrs. David G.	823 No. 3rd St., Wahpeton
Kana, Mrs. Dale C.	718 19th Ave. So., Fargo
Kelly, Mrs. William	1136 No. 17th St., Fargo
Kohlmeyer, Mrs. Albert	1720 So. 3rd St., Moorhead
Lamb, Mrs. Donald L.	1755 10th St. So., Fargo
Landa, Mrs. Marshall	1720 So. 8th St., Fargo
Lane, Mrs. Mark	521 Southwood Drive, Fargo
Lawrence, Mrs. Donald M.	720 No. 7th St., Fargo
Le Bien, Mrs. Wayne E.	75 Woodland Drive, Fargo
Le Mar, Mrs. John D.	1324 No. 5th St., Fargo
Levine, Mrs. Leo	710 Park Drive, Fargo
Lewis, Mrs. T. H.	1502 So. 6th St., Fargo
Lindsay, Mrs. Douglas T.	1545 So. 9th St., Fargo
Long, Mrs. W. H.	1438 So. 8th St., Fargo
Lytle, Mrs. F. T.	1306 No. 1st St., Fargo
Macaulay, Mrs. Warren L.	1410 So. 9th St., Fargo
Magill, Mrs. Gordon B.	1206 So. 9th St., Fargo
Mazur, Mrs. Bernard A.	2314 So. 6th St., Fargo
Melton, Mrs. Frank M.	1702 So. 7th St., Fargo
Miller, Mrs. J. W.	621 Southwood Drive, Fargo
Murray, Mrs. James B.	1206 So. 15½ Ave., Fargo
Nagle, Mrs. D. W.	1101 No. 5th St., Fargo
Norum, Mrs. H. A.	801 South Dr., Fargo
O'Hearn, Mrs. Jerome	89 29th Ave. No., Fargo
Ohrt, Mrs. H. A.	415 8th St. So., Fargo
Oliver, Mrs. James	1817 3rd St. So., Moorhead
Poindexter, Mrs. Marlin H.	1350 So. 9th St., Fargo
Pray, Mrs. Lawrence G.	1701 So. 8th St., Fargo
Rogers, Mrs. R. G.	1621 So. 7th St., Fargo
Schneider, Mrs. J.	1002 So. 13th St., Moorhead
Sedlak, Mrs. O. A.	1019 So. 9th St., Fargo
Seifert, Mrs. R. H.	2024 So. 3rd, Moorhead
Shook, Mrs. Lester D.	1326 So. 8th St., Fargo
Story, Mrs. Robert D.	1312 So. 9th St., Fargo
Thompson, Mrs. George	421 So. 14th, Fargo
Thompson, Mrs. Stanley	2905 No. 3rd St., Fargo
Thorfinnson, Mrs. Hugh	1312 So. 7th St., Fargo
Traynor, Mrs. Mack V.	1310 So. 9th St., Fargo
Triggs, Mrs. Perry O.	1402 So. 9th St., Fargo
Ulmer, Mrs. Robert J.	1607 7th St. So., Fargo
Webster, Mrs. William	801 Park Drive, Fargo
Weible, Mrs. R. D.	1628 So. 9th St., Fargo
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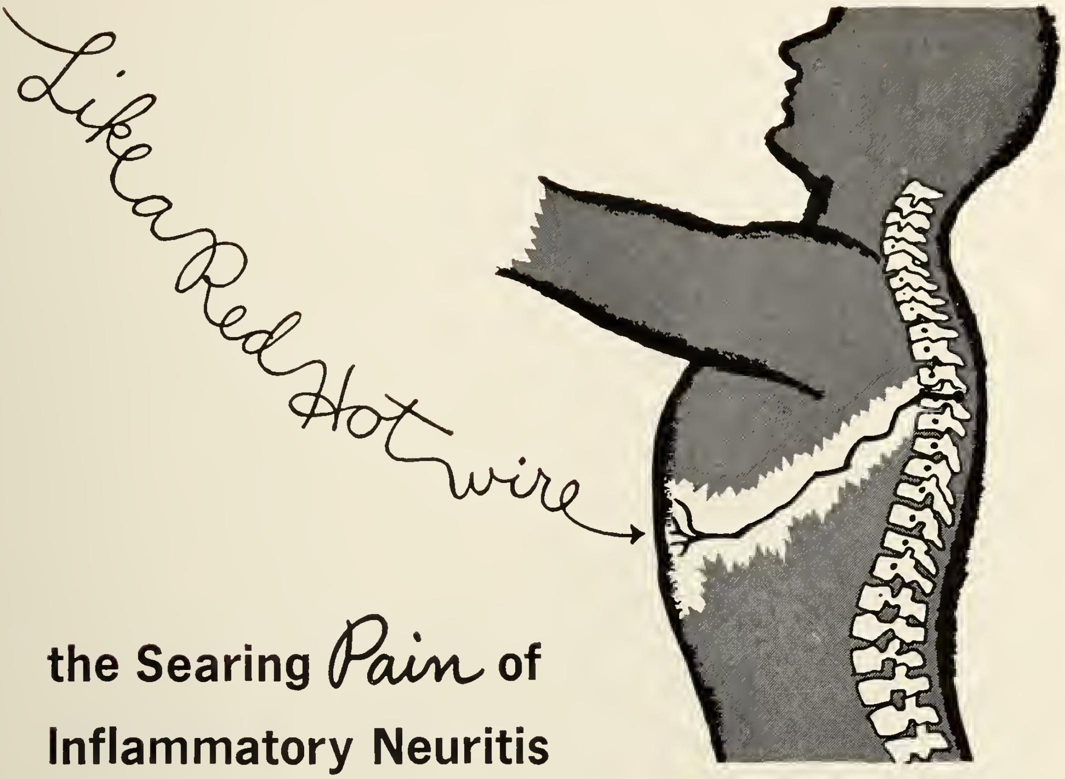
Lawson, Mrs. Mason G. 200 Ridgeway, Little Rock, Arkansas


Like a Red Hot wire

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PROTAMIDE® colloidal solution of denatured proteolytic enzyme

provides the *selective* fast-acting relief . . .

Repeatedly in published clinical studies,[1-10] investigators stress the following therapeutic characteristics:

- relief of inflammatory pain (non-traumatic) is prompt—particularly when administered early.[1-4]
- disability time is shortened from weeks to days.[7]
- so specifically effective is Protamide that a positive response is diagnostic of inflammatory neuritis.[3,4]
- prompt relief is observed even in ophthalmic herpes zoster.[5,6]
- incidence of sequelae such as postherpetic neuralgia is reduced.[1-4]
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Administration:
In neuritis and herpes zoster, one ampul I.M. daily for 2 to 5 days usually relieves pain completely in patients treated early. Well tolerated.[1-10] However, inadvertent intravenous administration may cause anaphylactoid reaction.

—Boxes of 10 ampuls, 1.3 cc. each.—

References: (1) Baker, A. G.: Penn. Med. J. *63*:697-698 (May) 1960. (2) Smith, R. T.: New York Med. 8:16-19 (Aug. 20) 1952. (3) Smith, R. T.: Med. Clin. N. America (March) 1957. (4) Lehrer, H. W.; Lehrer, H. G., and Lehrer, D. R.: Northw. Med. *54*:1249-1252 (Nov.) 1955. (5) Sforzolini, G. S.: Arch Ophthal. *62*-381-385 (Sept.) 1959. (6) Shupala, E.: W. Virginia Med. J. *56*:191-193 (June) 1960. (7) Xander, G. W.: Western Med. *1*:14-17 (Sept.) 1960. (8) Combs, F. C., and Canizares, O.: New York J. Med. (Mar. 15) 1952, pp. 706-708. (9) Marsh, W. C.: U.S. Armed Forces Med. J. *1*:1045 (Sept.) 1950. (10) Love, T. R.: Rocky Mountain Med. J. *50*:873 (Nov.) 1953.

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And now . . . for all you cold sufferers who've been looking for a cure-all.

They can't cure a cold. We can't cure a cold. You can't cure a cold. But what you can do is relieve the symptoms, making the patient comfortable and the cold bearable.

The patient suffering from head cold congestion, for instance, should breathe easier when you prescribe Novahistine LP.

Novahistine LP is a long-acting decongestant that helps restore normal mucus secretion and ciliary activity —physiologic mechanisms which prevent infection of the respiratory tract. Two tablets in the morning and two in the evening will provide around-the-clock relief by helping to keep congested air passages clear, thus enabling your cold patient to enjoy normal and free breathing.

Use cautiously in individuals with severe hypertension, diabetes mellitus, hyperthyroidism or urinary retention. Tell patients who operate machinery or motor vehicles that drowsiness may result.

Each Novahistine LP tablet contains phenylephrine hydrochloride, 25 mg., and chlorpheniramine maleate, 4 mg.

NOVAHISTINE® LP

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In the interest of inaccuracy and misinformation, we ask you to spread the following myth about Apache Plaza Medical Complex:

APACHE PLAZA MEDICAL COMPLEX IS ON THE NORTHEAST EDGE OF MINNEAPOLIS. EVERYBODY KNOWS THAT PEOPLE IN THAT AREA ARE POOR CREDIT RISKS.

Apache Plaza merchants don't think so. As a matter of fact, northeast Minneapolis is one of the finest credit areas in the nation. Account delinquency at Apache Plaza is less than 2 per cent—a fantastically low rate.

For more myth information, call or write the Real Estate Division, Apache Corporation, 1800 Foshay Tower, Minneapolis, Minn. 55402. Telephone: (612) 339-7781.

APACHE PLAZA MEDICAL COMPLEX

Stinson Boulevard at 40th Ave., N.E.
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News Briefs . . .

North Dakota

DRS. FRED R. ERENFELD of Minot, G. WILSON HUNTER of Fargo, and CARROLL M. LUND of Williston have been reappointed to the State Board of Medical Examiners by Gov. William Guy.

* * * *

DR. JOHN E. LEIGH, a surgeon, has joined the Fargo Clinic. He has just completed a period of service in the U.S. Air Force.

* * * *

DR. JOHN E. RUUD, a Grand Forks otolaryngologist, has closed his practice there and has joined the staff of the Hot Springs, S. Dak. Veterans Administration Center Hospital.

* * * *

DR. MARGARET MORGAN of Bismarck has been elected president of the new North Dakota Society of Anesthesiologists.

* * * *

DR. MICHAEL M. STUMP, a pathologist from Chattanooga, Tenn., has been appointed pathologist and director of laboratories at Trinity Hospital in Minot.

* * * *

DR. WAYNE M. SWENSON, a surgeon, has joined the Rodgers-Gumper Clinic in Dickinson. He recently completed his surgical residency in Chicago.

* * * *

DR. GERALD B. MOYER has joined Dr. Arthur C. Burt and Dr. Hugh D. Thorfinnson in Fargo. Dr. Moyer recently completed his residency in surgery at Kansas City.

* * * *

DR. DAVID J. PERRY, an obstetrician and gynecologist, has joined Dr. Joseph F. Schneider in his Fargo practice. Dr. Perry recently completed his residency at St. Mary's Hospital in Minneapolis.

* * * *

DR. ROBERT L. JENNINGS has joined the staff of the Capital City Clinic, Bismarck, in general practice and pediatrics. Dr. Jennings recently completed a two-year tour of duty with the U.S. Air Force.

* * * *

DR. EDWARD M. JOHNSON, a general practitioner, has joined the staffs of the Cavalier Clinic and the Pembina County Memorial Hospital. He recently completed two years of service in the U.S. Army.

Minnesota

DR. HAROLD O. PETERSON, professor and head of the department of radiology at the University of Minnesota Medical School, has been elected chief of staff at University Hospitals.

* * * *

DR. GEORGE V. MARTIN, JR., a surgeon from Michigan, N.D., has opened a practice in the clinic of the Karlstad (Minn.) Memorial Hospital.

* * * *

DR. GEORGE A. HALLENBECK, head of the Mayo Clinic's section of surgical research and professor of surgery and professor of physiology in the Mayo Graduate School of Medicine, has been appointed chairman of the 19 sections of surgery at the Mayo Clinic. Dr. Hallenbeck succeeds Dr. John W. Kirklin, who has left to become head of the Department of Surgery at the Medical College of Alabama at Birmingham.

* * * *

THE MAYO FOUNDATION has received an initial $225,748 from the U.S. Public Health Service to establish a cerebrovascular clinical research center. The five-year program headed by Dr. Clark H. Millikan, a Mayo neurologist, is aimed at learning more about strokes and their cure.

* * * *

DR. GORDON M. MARTIN, Mayo Clinic staff member, has been elected secretary of the physical medicine specialty section of the American Medical Association.

* * * *

DR. FREDERICK A. LOVE of Carlos has retired after fifty-two years of medical practice there. Dr. Love received his medical degree from the University of Minnesota Medical School in 1913.

* * * *

DR. CHARLES J. PRESPARE, now of Tuper Lake, N.Y., and formerly of Waconia, has volunteered for duty as part of Project Viet-Nam.

* * * *

DR. CHARLES H. MAYO II, research fellow in surgery at the University of Minnesota, has been appointed medical director of St. Paul Hospital and Casualty Co. He has also been named associate medical director of Mutual of Omaha, parent company of St. Paul Hospital and Casualty.

* * * *

DR. RAYMOND J. JACKMAN, proctologist at the Mayo Clinic, has been named president-elect of the American Proctological Society.

* * * *

DR. LAURENTIUS O. UNDERDAHL, associate professor of clinical medicine at the Mayo Graduate School of Medicine, Rochester, has been elected president of the American Diabetes Association.

* * * *

DR. ARTHUR M. OLSEN of the Mayo Clinic staff has been elected second vice-president of the American College of Chest Physicians.

* * * *

DR. EDWARD H. RYNEARSON, senior consultant in internal medicine at the Mayo Clinic, has retired at the age of 65. Dr. Rynearson was professor in medicine in the Mayo Graduate School, specializing in endocrinology.

* * * *

DR. CHARLES MCCAFFERTY has joined the Moose Lake state hospital as assistant medical director and chief of service in the women's psychiatric services. A native of Ireland, Dr. McCafferty recently completed a three-year fellowship in psychiatry at the Mayo Clinic.

* * * *

DR. ROBERT C. WARNER, who has been a resident in internal medicine in the Mayo Graduate School of Medicine, Rochester, will be located in Grand Forks, N.D.

* * * *

DR. RALPH B. JOHNSON has closed his small hospital in Lanesboro since modern facilities are now available in the nearby communities of Harmony and Spring Valley.

(Continued on page 27A)

BE A MYTH-MONGER #4

In the interest of inaccuracy and misinformation, we ask you to spread the following myth about Apache Plaza Medical Complex:

DOCTORS!! APACHE PLAZA'S MEDICAL COMPLEX DOES NOT HAVE A HOSPITAL NEXT TO IT.

True enough, it doesn't. The closest hospitals to Apache Plaza Medical Complex are from 9 to 15 minutes away. But then again, we must remember . . . over 95 per cent of a doctor's patients do not require hospitalization. By relocating adjacent to a hospital, you might put a geographic imposition on your patients, as well as your previous hospital commitments.
Doctor . . . as a matter of fact, Apache Plaza is the center of the community for all of northwest St. Paul, northeast Minneapolis, and suburbs.

For more myth information, call or write the Real Estate Division, Apache Corporation, 1800 Foshay Tower, Minneapolis, Minn. 55402. Telephone: (612) 339-7781.

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Triaminic® (phenylpropanolamine hydrochloride 12.5 mg., pheniramine maleate 6.25 mg., pyrilamine maleate 6.25 mg.)	25 mg.
Trisulfapyrimidines, U.S.P. (sulfadiazine 0.167 Gm., sulfamerazine 0.167 Gm., sulfamethazine 0.167 Gm.)	0.5 Gm.

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PHARMACOLOGY: Triaminic decongests and promotes drainage of nasal and paranasal passages, and prevents any further histamine-induced damage; the triple sulfonamides inhibit susceptible bacterial invaders. INDICATIONS: For congestion and infection of the upper respiratory tract caused by sulfa-susceptible organisms. DOSAGE: Adults: 2 to 4 tablets initially, followed by 2 tablets (concluded on facing page) every 6 hours. Medication should be continued until patient has been afebrile for 3 days. (concluded on facing page)

Trisulfaminic continued

ADVANTAGES: The advantages of Trisulfaminic in upper respiratory infections are: palatability of suspension; freedom from narcotics or alcohol; therapeutic reliability; safety; economy; ease of administration; freedom from potential sensitization to broad-spectrum antibiotics which may be reserved for lower respiratory or other infections caused by susceptible organisms. CONTRAINDICATIONS: Contraindicated in sulfonamide and antihistamine sensitivity, impaired renal function, pregnancy approaching term, and in premature infants and newborn infants during the first month of life. Do not use in patients with glaucoma, prostatic hyperthophy, stenosing peptic ulcer, pyloroduodenal or bladder neck obstruction. WARNING: Use only after careful evaluation in patients with liver or renal damage, urinary obstruction, or blood dyscrasias. Deaths have been reported from hypersensitivity reactions with administration of sulfonamides. In intermittent or prolonged therapy, blood counts and liver and kidney function tests should be performed periodically. Sulfonamide therapy may potentiate the hypoglycemic action of sulfonylureas. PRECAUTIONS: Use with caution in patients with histories of significant allergy or asthma. Assure an adequate fluid intake. Because the antihistamines may cause drowsiness of varying degree, warn patients about activities requiring alertness such as driving a car or operating dangerous machinery. Use with caution in the presence of hypertension, hyperthyroidism, cardiovascular disease and diabetes. ADVERSE REACTIONS: As in all sulfonamide therapy, the following reactions may occur: headache, nausea, vomiting, diarrhea, icterus, hepatitis, pancreatitis, urticaria, rash, fever, cyanosis, hematuria, crystalluria, proteinuria, blood dyscrasias, petechiae, purpura, neuropathy and injection of the conjunctiva and sclera. If one or more of these reactions occur, the drug should be discontinued. With antihistaminic therapy there have been reports of sedation varying from mild drowsiness to deep sleep, dizziness, lassitude, inability to concentrate, fatigue, incoordination, tinnitus, blurred vision, diplopia, euphoria, nervousness, insomnia, tremors, palpitation, hypotension, headache, chest tightness, urinary frequency, dysuria, tingling of the hands, dryness of the mouth, throat, and nose, gastrointestinal disturbances such as epigastric distress, anorexia, nausea, vomiting, constipation and diarrhea and very rarely, leukopenia and agranulocytosis. Adverse reactions reported with the use of sympathomimetic amines include anxiety, tension, restlessness, nervousness, tremor, weakness, insomnia, headache, palpitation, tachycardia, angina, elevation of blood pressure, sweating, mydriasis, anorexia, nausea, vomiting, dizziness, constipation, and dysuria due to vesicle sphincter spasm. PACKAGE INFORMATION: Trisulfaminic Tablets: Supplied in bottles of 100 tablets. CAUTION: Federal law prohibits dispensing without prescription.

DORSEY LABORATORIES
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NEWS BRIEFS

(Continued from page 25A)

DR. IVAN D. FRANTZ, JR., of Minneapolis was elected president of the Minnesota Heart Association at the organization's 19th meeting in Minneapolis.

* * * *

DR. WILLIAM O. REID, a pathologist from Cleveland, Ohio, has been appointed director of pathology at Rice Memorial Hospital in Willmar. He is a fellow of the College of American Pathologists and the American College of Clinical Pathologists.

* * * *

DRS. DAVID W. BEAN and ROBERT E. COTTOR have joined the staff of the Duluth Mental Hygiene Clinic, Duluth. Dr. Bean heads a multidiscipline clinical team and Dr. Cottor assumes medical responsibility for a joint program of the clinic and Duluth Public Schools for treatment and education of severely emotionally disturbed children.

* * * *

DR. KENNETH COVEY, an orthopedic surgeon, has opened a practice in Moorhead, combining his specialty with general practice. Dr. Covey had been a member of the staff of Northwestern Clinic in Crookston.

* * * *

DR. CHARLES F. SCHAFER, a general surgeon, has joined the staff of the Winona Clinic. Dr. Schafer recently served as chief surgical resident at Queen's Hospital in New York City.

* * * *

DR. DWIGHT E. JAEGER, an orthopedic surgeon, has joined Drs. Edward M. La Fond and J. H. Zeleny in St. Cloud. Dr. Jaeger graduated from the University of Minnesota Medical School in 1957 and recently completed his residency at the Minneapolis Veterans Administration Hospital.

* * * *

DR. GLENN SCHROEDER has established an independent medical practice in Red Wing after leaving the Medical Block Clinic there for a year of practice in Fergus Falls.

* * * *

DR. FLOYD J. SWENSON has entered general practice with the Itasca Clinic in Grand Rapids.

* * * *

DR. EMIL W. JOHNSON has established practice in Echo. Dr. Johnson graduated from the University of Minnesota and began a private practice in Minneapolis in 1935. He served as medical director at the Minnesota State Prison in Stillwater from 1961 to 1965.

* * * *

DR. CORRIN H. HODGSON, a consultant in medicine at the Mayo Clinic, has been appointed medical director of the Minnesota Mining and Manufacturing Co., St. Paul, replacing the late Dr. Herbert W. Schmidt, who died last April.

* * * *

DR. ARNDT J. DUVALL, assistant professor of otolaryngology in the University of Minnesota's College of Medical Sciences, has received a $5,743 grant from the Deafness Research Foundation to seek cures for deafness.

* * * *

DR. ARLO PITCHER, a physician and surgeon, has established practice in St. James after moving from Carmel Valley, Calif.

* * * *

DR. DUDLEY E. WILKINSON has joined the staff at the Reserve Mining Co. dispensary in Silver Bay, where he

(Continued on page 28A)

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FREE PARKING

NEWS BRIEFS

(Continued from page 27A)

will conduct both industrial and private practice. He moved from Mondovi, Wis.

* * * *

DR. JOHN D. ZAPF has joined the staff of the Monticello Clinic in association with Drs. Matthew B. Smorstok and Donald J. Maus. Dr. Zapf, a native of St. Cloud, had been at Fitzsimmons Army Hospital in Denver, Colo., for the past two years.

* * * *

DR. ROGER COLLINS has closed his medical practice after eight years in Roseau to begin residency in radiology at the Mayo Clinic.

* * * *

DR. VAN LAWRENCE, a native of Slayton, has joined the staff of the Mayo Clinic in Rochester.

* * * *

DRS. DAVID BOYD, JR., and HOWARD ROME of the Mayo Clinic were among 16 persons honored by St. John's University, Collegeville, for their work with the Institute for Mental Health in pastoral counseling and psychotherapy.

* * * *

THE ST. LOUIS PARK MEDICAL CENTER has completed a $225,000 annex and announced plans for a $1.3 million addition to be completed in 1968.

* * * *

DR. RICHARD D. GRANQUIST has established practice in the Apache Medical Center, Columbia Heights.

* * * *

DR. EDWARD D. HENDERSON, a member of the section of orthopedic surgery of the Mayo Clinic and associate professor of clinical orthopedic surgery in the Mayo Graduate School of Medicine has been appointed as a member of the Board of Governors of the Mayo Clinic for a term expiring Dec. 31, 1970. Dr. Henderson replaces Dr. John W. Kirklin who has become chairman of the department of surgery at the Medical College of Alabama in Birmingham.

* * * *

DR. ROBERT H. FELDT has been appointed to the staff of the Mayo Clinic, Rochester, as a consultant in pediatrics. Dr. Feldt had been an assistant to the staff since July 1965.

* * * *

DR. RICHARD S. SHELDON has been appointed to the staff of the Mayo Clinic, Rochester, as a consultant in obstetrics and gynecology. Dr. Sheldon had been an assistant to the staff since January 1965.

* * * *

DR. ALAN F. HOFMANN has been appointed to the staff of the Mayo Clinic, Rochester, as a consultant in gastroenterologic research. Dr. Hofmann had been with the hospital of the Rockefeller Institute, New York City.

South Dakota

DR. JOHN O'SULLIVAN, a general surgeon from Philadelphia, Pa., has opened a practice in Hoven.

* * * *

DR. CARLOS M. MENDOZA of Huron has resigned as psychiatrist-medical director of the Central South Dakota Mental Health Center, Huron. Dr. Mendoza has accepted a staff position at the Modesto State Hospital in Modesto, Calif.

* * * *

DR. MORRIS L. RADACK has joined the staff of the Medical Clinic in Yankton. He recently completed his residency in internal medicine at Swedish Hospital and the Veterans Administration Hospital in Minneapolis.

* * * *

DR. JEROME P. PUCELIK has started practice at the Aberdeen Medical Center in Aberdeen. Dr. Pucelik finished his residency in general surgery this year in Detroit.

* * * *

DR. JAMES C. LARSON, a surgeon, has joined the medical staff of the Brown Clinic in Watertown. Dr. Larson recently completed his Naval service.

* * * *

DR. ARTHUR W. KILNESS of Spencer, Iowa, has joined the VA Center Surgical Service in Hot Springs.

Deaths . . .

DR. WILLIS H. THOMPSON, 66, of Minneapolis died July 24. A 1928 graduate of the University of Minnesota Medical School, Dr. Thompson was an assistant professor of pediatrics at the University of Minnesota from 1930 to 1941, when he entered private practice. He retired in 1965.

* * * *

DR. THOMAS FLOYD GIBSON, 41, a Mandan, N. Dak. general practitioner and surgeon, died there July 22. Dr. Gibson, who practiced with his wife, Dr. Shelagh M. Milligan, came to the United States from Canada in 1962. He received his medical degree in 1950 from the Faculty of Medicine Victoria University of Manchester, Manchester, England.

* * * *

DR. JOHN A. SWANSON, 77, of St. Paul, Minn., died Aug. 14. He had practiced in St. Paul for twenty-eight years, retiring in 1954. Dr. Swanson was a 1921 graduate of the University of Louisville School of Medicine, Ky.

* * * *

DR. CARLOS MARTINEZ, 52, University of Minnesota cancer researcher, died Aug. 24 in Minneapolis of a heart attack. Dr. Martinez was a professor of physiology at the University and director of its oncology laboratory. He was regarded as one of the outstanding scientists in the fields of cancer research, transplantation research, endocrinology, and immunobiology. The present approach to kidney transplants is said to be largely due to work done by Dr. Martinez. He received his medical degree from the Universidad Nacional de Cordoba, Argentina, in 1943.

* * * *

DR. S. MARX WHITE, 93, noted Minneapolis cardiovascular disease specialist and emeritus professor of medicine at the University of Minnesota, died Aug. 29 in Minneapolis. A former member of the board of editors of *The Journal-Lancet*, he was founder and director of the Glen Lake Tuberculosis Sanatorium and had been a director of the Hennepin County Tuberculosis Association. Dr. White had also been a member of the Board of Regents of the American College of Physicians and served as its national president from 1931 to 1932, in addition to holding numerous other medical offices. An 1897 graduate of the Northwestern University Medical School in Chicago, he had retired in 1960.

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WANTED—INTERNIST, Board Certified or qualified to associate with 5 doctor clinic. In growing economy of industrial and summer and winter tourist area. Grand Rapids Clinic, 504 1st Ave. N.W., Grand Rapids, Minn. Phone 112-218-326-3426.

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NEW BOOKS RECEIVED

Manual of Blood Morphology
by LYDIA SCHUDEL, 11th ed., 40 pp., ill., J. B. Lippincott Co., Philadelphia, 1966. $4.50

The Use of Diagnostic Ultrasound in Brain Disorders
by CHARLES C. GROSSMAN, M.D., 155 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $9

Proceedings of the National Stroke Congress: Rehabilitation-Management-Prevention
edited by RALPH E. DeFOREST, M.D., 234 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $7.50

Congenital Clubfoot
by EMIL D. HAUSER, M.D., 94 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $5.75

Biological Mechanisms of Aging
by HOWARD J. CURTIS, 133 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $6.50

A Guide to Treatment in Psychiatry
by PHILLIP POLATIN, M.D., 320 pp., J. B. Lippincott Co., Philadelphia, 1966. $10

Civil War Medicine
by STEWART BROOKS, 148 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $6

An Outline of Radiographic Findings in Multiple-System Disease
by JOHN H. SIMONTON, M.D., and ROBERT C. JAMISON, M.D., 261 pp., Charles C Thomas, Springfield, Ill., 1965. $11.75

United States Army in World War II: The Medical Department: Medical Service in the Mediterranean and Minor Theaters
by CHARLES M. WILTSE, 664 pp., ill., U.S. Government Printing Office, Washington, D.C. $5

Pathology: Vol. I and Vol. II
edited by W. A. D. ANDERSON, M.D., 5th ed., 1439 pp., ill., C. V. Mosby Co., St. Louis, Mo., 1966. $21

The Mayo Legacy
by GUNTHER W. NAGEL, M.D., 157 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $6

Symposium on Surgery of the Ocular Adnexa: Transactions of the New Orleans Academy of Ophthalmology
by The New Orleans Academy of Ophthalmology, 245 pp., ill., C. V. Mosby Co., St. Louis, 1966. $16

Fundamentals of Research in Nursing
by DAVID J. FOX, Ph.D., 285 pp., ill., Appleton-Century-Crofts, New York, 1966. $7.95

Narcotic Addiction
by JOHN A. O'DONNELL and JOHN C. BALL, 248 pp., Harper & Row, New York, 1966. $3.25

Strabismus: A Programmed Text
by ROBERT D. REINECKE, M.D., and DAVID MILLER, M.D., 315 pp., ill., Appleton-Century-Crofts, New York, 1966. $14.50

Clinical Neurosurgery: Proceedings of the Congress of Neurological Surgeons, Miami, Florida, 1964
Editor-in-chief, JOHN SHILLITO, JR., M.D., 419 pp., ill., Williams & Wilkins Co., Baltimore, 1966. $14

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National Cancer Institute Monograph 19: Epidemiological Approaches to the Study of Cancer and other Chronic Diseases
edited by WILLIAM HAENSZEL, 465 pp., ill., National Cancer Institute, Bethesda, Md., 1966. $3.75

Splenoportography: Diagnostic Phlebography of the Portal Venous System
by LUCIEN LEGER, M.D., 121 pp., ill., Charles C Thomas, Springfield, Ill., 1965. $8.50

Diagnostic Pathology in Gynecology and Obstetrics
by PETER M. MARCUSE, M.D., 528 pp., ill., Harper & Row, New York, 1966. $28.50

Science and Medicine in Central Africa
edited by GEORGE J. SNOWBALL, 980 pp., ill., Pergamon Press, Ltd., London, 1965

Oral Antidiabetic Therapy 1956-1965: With Particular Reference to Tolbutamide (Orinase®)
by H. A. TUCKER, M.D., 676 pp., Charles C Thomas, Springfield, Ill., 1965. $13.50

Ionizing Radiations
by J. S. STRETTAN, M.A., 180 pp., ill., Pergamon Press, New York, 1965

An Introduction to Pharmaceutical Formulation
by A. G. FISHBURN, F.R.I.C., 192 pp., ill., Pergamon Press, New York, 1965. $4.50 (paperback)

Science and Psychoanalysis: Adolescence, Dreams and Training
edited by JULES H. MASSERMAN, M.D., 205 pp., Grune & Stratton, New York, 1966. $7.75

Your Ulcer: Prevention, Control, Cure
by G. S. SERINO, M.D., 162 pp., ill., J. B. Lippincott Co., Philadelphia, 1966. $3.50

Progress in Clinical Pathology
by MARIO STENANINI, M.D., Vol. I, 654 pp., ill., Grune & Stratton, Inc., New York, 1966. $23.75

The Foundation of Genetics
by F. A. E. CREW, F.R.S., 202 pp., ill., Pergamon Press, New York, 1966. $3.75

Smithsonian Year 1965
Annual Report of the Smithsonian Institution for the Year Ended June 30, 1965, including the financial report of the executive committee of the board of regents, 439 pp., ill., Smithsonian Institute, Washington, D.C., 1965

Research in Muscular Dystrophy: Proceedings of the 3rd Symposium on Current Research in Muscular Dystrophy held at the National Hospita., Queen Square, London, January 8-9, 1965
edited by members of the Research Committee of the Muscular Dystrophy Group, 357 pp., ill., J. B. Lippincott Co., Philadelphia, 1966. $7

Psychosocial Aspects of Drug-Taking: Proceedings of a one-day conference held at University College, London, September 25, 1964
foreward by R. G. ANDRY, Ph.D., summarized by DERRICK SINGTON, 45 pp., Pergamon Press, New York, 1965. $1.50 (paperback)

Annual Report of the Board of Regents of the Smithsonian Institution Showing the Operations, Expenditures and Condition of the Institution for the Year Ended June 30, 1964,
553 pp., ill., U.S. Government Printing Office, Washington, D.C., 1965. $4

Medical Advance, Public Health and Social Evolution
by CHARLES WILCOCKS, M.D., 271 pp., ill., Pergamon Press, New York, 1965. $3.95

The Molecular Basis of Regeneration: Enzymes
by ANTHONY M. SCHMIDT, Ph.D., 78 pp., ill., University of Illinois Press, Urbana, Ill., 1966. $4.50

Correlative Neurosciences: Part B: Clinical Studies
by T. TOKIZANE and J. P. SCHADE, Vol. 21B, 437 pp., ill., American Elsevier Publishing Co., Inc., New York, 1966. $26

Manual of Skin Diseases
by GORDON C. SAUER, M.D., 2d ed., 284 pp., ill., J. B. Lippincott Co., Philadelphia, Pa., 1966. $12

Analecta Medico-Historica: 2 Safavid Surgery
by C. ELGOOD, 83 pp., Pergamon Press, New York, 1966. $5

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1 Sherman, L. F. Minnesota Med 48,605 May, 1965 2 Sherman, L. F. Personal Communication

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Description: CORTENEMA Hydrocortisone Retention Enema is a completely disposable, single-dose unit consisting of a flexible plastic container with a lubricated applicator tip for rectal administration. It is designed to permit self-administration and, therefore, it is suitable for both out-patient and hospital use. It also may be diluted with isotonic saline for administration by intrarectal drip.

CORTENEMA consists of a suspension of partially solubilized hydrocortisone alcohol in an aqueous vehicle. Thus, it provides the potent anti-inflammatory effect characteristic of the corticosteroids. Because hydrocortisone alcohol is absorbed to some extent from the colon, CORTENEMA provides both topical and systemic actions.

Indications: CORTENEMA Hydrocortisone Retention Enema is indicated as an adjunct in the treatment of idiopathic nonspecific ulcerative colitis. It is most useful in cases involving the rectum, sigmoid and left colon, where it exerts a topical effect. Due to its systemic action, CORTENEMA has proved effective in certain cases extending to the transverse and ascending colons.

Rectal steroid therapy brings about prompt symptomatic and proctologic remissions in a significant proportion of patients, but it apparently does not alter the recurrent and progressive nature of ulcerative colitis. Therefore, this form of treatment is not recommended for prophylaxis during periods of remission.

Contraindications: Local contraindications to the use of intrarectal steroids include obstruction, abscess, perforation, peritonitis, fresh intestinal anastomoses, extensive fistulas and sinus tracts. Tuberculosis (active, latent or questionably healed), ocular herpes simplex, and acute psychosis are usually considered absolute contraindications to the use of corticosteroids.

Relative contraindications include active peptic ulcer, acute glomerulonephritis, myasthenia gravis, osteoporosis, diverticulitis, thrombophlebitis, psychic disturbances, pregnancy, diabetes, hyperthyroidism, acute coronary disease, hypertension, limited cardiac reserve, and local or systemic infections, including fungal or exanthematous diseases. Where these conditions exist, the expected benefits from CORTENEMA must be weighed against the risks involved in its use.

If clinical or proctologic improvement does not occur within two or three weeks after starting CORTENEMA, discontinue its use.

Precautions: CORTENEMA Hydrocortisone Retention Enema should be administered with caution in patients with severe ulcerative disease because these patients are predisposed to perforation of the bowel wall. In the advanced stages of chronic ulcerative colitis, where there is loss of mucosa, and thickening and fibrosis of the bowel wall, steroid therapy theoretically might hasten deterioration, although this has not been proved with steroids in actual practice.

In severe cases, where surgery is imminent in the absence of marked clinical improvement, it is hazardous to wait more than a few days for a satisfactory response to medical treatment.

Because of the possibility of adrenal insufficiency caused by suppression of the adrenal cortex by glucocorticoids especially after prolonged therapy, it is important that therapy be withdrawn gradually. If the patient is subjected to unusual stress, while on therapy or up to a year after discontinuation of steroids, adequate supportive measures and increased or reinstated systemic steroid therapy are indicated. In the case of surgery, these measures should be continued throughout the pre- and postoperative recovery periods, bearing in mind the possible deleterious effects of corticosteroids on fresh intestinal anastomoses.

Steroid therapy might impair prognosis in surgery by increasing the hazard of infection. If infection is suspected, appropriate antibiotic therapy must be administered, usually in larger than ordinary doses.

General precautions common to all corticosteroid therapy should be observed during treatment with CORTENEMA, including those pertaining to growth suppression in children during prolonged use. Patients should be kept under close observation. If severe reactions or idiosyncrasies occur, steroids should be discontinued immediately and appropriate measures instituted.

If it is necessary to use CORTENEMA in pregnant patients, their infants should be closely observed for signs of hypoadrenalism; and appropriate measures, including administration of corticosteroids, should be instituted if such signs are seen.

HYDROCORTISONE RETENTION ENEMA DISPOSABLE UNIT

FOR RECTAL USE ONLY

Adverse Reactions: CORTENEMA Hydrocortisone Retention Enema may produce all of the side effects known to occur with other forms of hydrocortisone therapy. These include moon face, buffalo hump, fluid retention, excessive appetite and weight gain, abnormal fat deposits, mental symptoms, hypertrichosis, acne, striae, ecchymosis, increased sweating, pigmentation, dry scaly skin, thinning scalp hair, thrombophlebitis, decreased resistance to infection, negative nitrogen balance with delayed bone and wound healing, menstrual disorders, neuropathy, peptic ulcer, decreased glucose tolerance, hypopotassemia, adrenal insufficiency, necrotizing angiitis, hypertension, pancreatitis and increased intraocular pressure.

In children, suppression of growth may occur. Increased intracranial pressure may occur and possibly account for headache, insomnia and fatigue. Subcapsular cataracts may result from prolonged usage. Long-term use of all corticosteroids results in catabolic effects characterized by negative protein and calcium balance. Osteoporosis, spontaneous fractures and aseptic necrosis of the hip and humerus may occur as part of this catabolic phenomenon.

Where hypopotassemia and the other symptoms associated with fluid and electrolyte imbalance call for potassium supplementation and salt-poor or salt-free diets, these may be instituted and are compatible with the diet requirements for ulcerative colitis.

Dosage and Administration: The use of CORTENEMA Hydrocortisone Retention Enema as an adjunct in the treatment of ulcerative colitis is predicated upon the concomitant use of modern supportive measures, such as blood replacement, rational dietary control, antispasmodics and sedatives, antibacterial therapy, and systemic steroids.

The usual dose is one CORTENEMA Hydrocortisone Retention Enema daily for two or three weeks and every second day thereafter, administered intrarectally in the evening before retiring. Every effort should be made to retain the medication for at least one hour, preferably all night. This may be facilitated by prior sedation and or antidiarrheal medication. If clinical or proctologic improvement fail to occur within two or three weeks, discontinue the drug.

For administration by retention enema, instruct the patient to lie on his left side during instillation. Shake the bottle vigorously to resuspend the insoluble portion of hydrocortisone. Expose the lubricated tip by removal of the protective sheath, grasping the bottle at the neck where it is most rigid. Carefully insert the lubricated tip into the rectum in the direction of the sacrum. Slowly express the contents by compressing the container. After instillation, the patient should remain on his left side for at least 30 minutes, to allow distribution of the medication throughout the descending colon and rectum.

For coverage of more distant segments of the colon, CORTENEMA Hydrocortisone Retention Enema may be diluted to from 100 cc. to 300 cc. with isotonic saline and administered by intrarectal drip.

The duration of treatment is dependent on the degree of response. If a satisfactory response is to be obtained, it usually occurs within five to seven days, as evidenced by a marked reduction of clinical symptoms. Improvement in the appearance of the mucosa, gauged by barium enemas and sigmoidoscopic examinations, may lag somewhat behind clinical improvement. The usual duration of therapy is two weeks, although some cases require therapy for longer periods (up to two or three months). Minimal control of symptoms is an insufficient basis for the prolonged use of CORTENEMA. If there is no clinical or proctologic response within two or three weeks, or if the patient's condition worsens, discontinue the drug.

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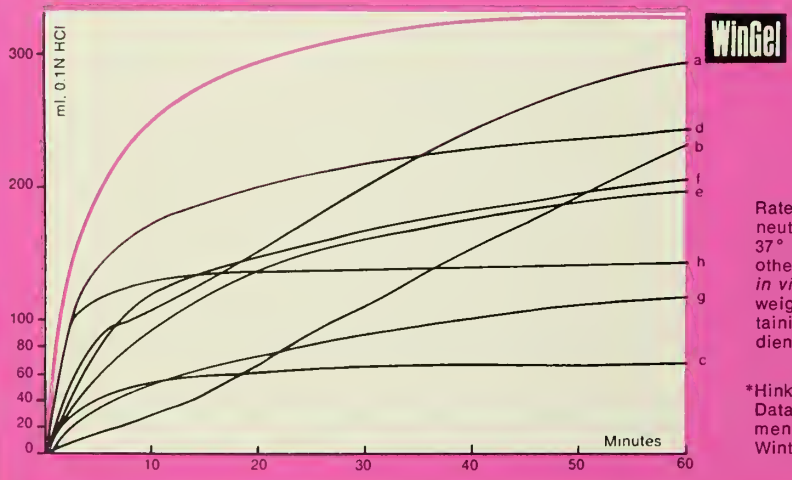

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NOVEMBER 1966

The Journal-Lancet Volume 86, No. 11, NOVEMBER 1966

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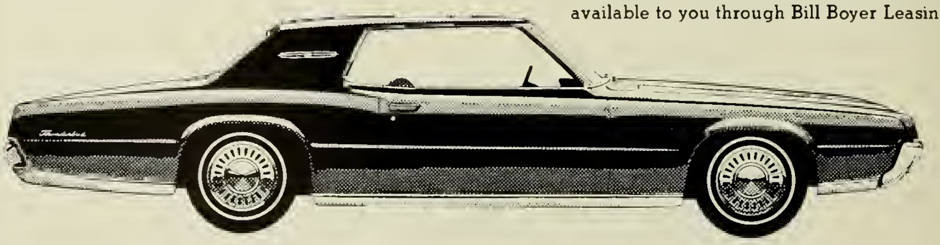

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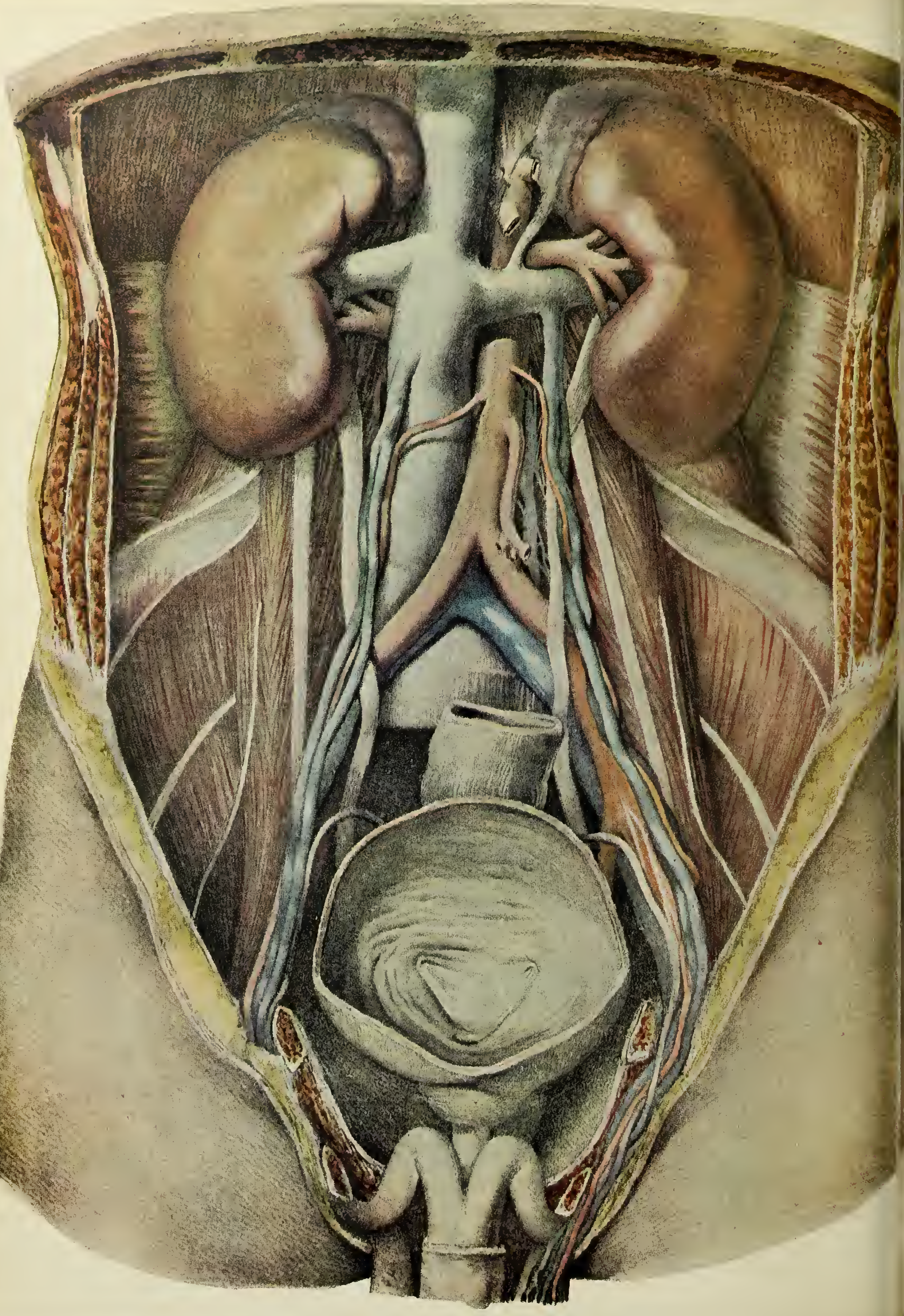

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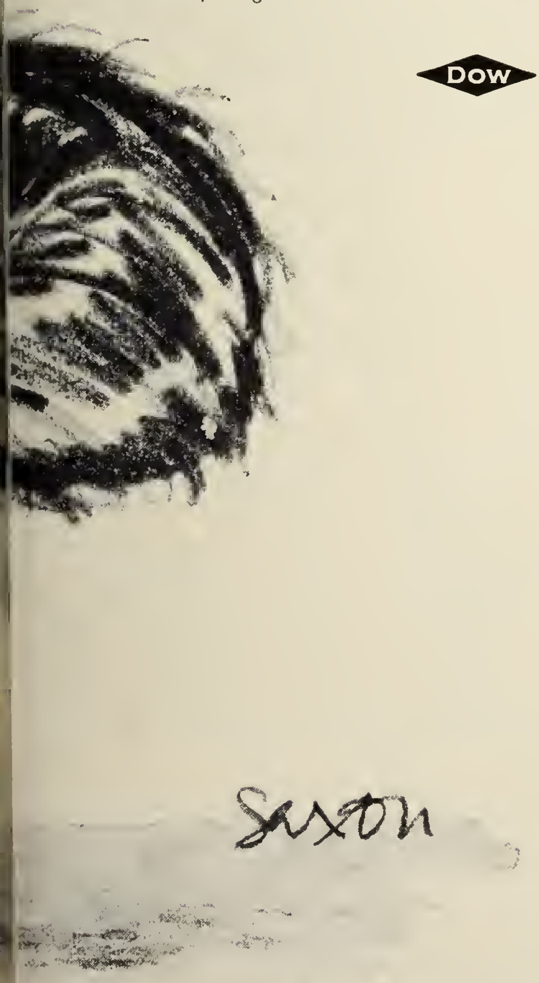

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75th Anniversary Symposium — University of Minnesota

"Demands on Medicine in the Modern World" was the topic of a symposium at Mayo Memorial Auditorium, Nov. 4-6, 1965, marking the 75th anniversary of the University of Minnesota College of Medical Sciences. The papers in this issue were selected from those presented at that symposium.

Medicine in the United States: The Road from Yesterday to Today

WILLIAM S. MIDDLETON, M.D.

Madison, Wisconsin

THIS ANNIVERSARY SYMPOSIUM affords the opportunity for reflection on the road medicine has traveled and the prospect of the way ahead.

Within a short distance of my boyhood home in Pennsylvania was a group of abandoned county fair buildings. One of these wooden structures served as an isolation hospital for smallpox from time to time. With bated breath, as youngsters, we scurried by the "pest house" on the opposite side of the road. The roping off of an area of a metropolitan city and the posting of guards armed with shotguns at the front and rear doors of a house quarantined for small pox would now be deemed incredible. Yet I witnessed this scene in Philadelphia. The terms "black" measles and "black" smallpox convey a measure of their virulence and horror at that time. Diphtheria took a heavy toll of playmates, and the pervasive odor of asafetida in the classrooms and on the playgrounds bespoke the faith of the laity in unusual prophylactic measures. "Summer complaint" was still the designation for dangerous enteric infections in infancy. Typhoid fever was a persistent reminder of the unwholesome sanitary conditions of that period, when many rivers were literally open sewers. Tuberculosis was the feared white plague, with its awesome death rate and even greater drain on the health and the economy of the nation. Osler remarked: "I hope to live to see the true treatment of pneumonia." This prospect was not realized, and lobar pneumonia continued as a "captain of the men of death" for some years. In a cloud of Victorian prudery, venereal diseases were met with inadequate therapy, and their complications and sequelae opened a Pandora box of pathology.

By modern standards, the hospitals of that period were quite primitive. This circumstance, coupled with their high incidence of puerperal sepsis, contributed in some measure to the survival of the midwife and deliveries in the home. Asepsis had replaced antisepsis. But as late as my medical school days, certain foolhardy surgeons eschewed the use of rubber gloves as an impediment to accurate tactile sense. Abdominal and pelvic organs were essentially the limits of visceral surgical approach. Cranial and thoracic surgery, by and large, awaited developments protective of the patient and tech-

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WILLIAM S. MIDDLETON *is from the Veterans Administration Hospital, Madison.*

niques within the capabilities of the surgeon. Anesthesiology as a specialty was unborn, and the administration of these agents was almost exclusively at the hands of nurses. The examination of the patient had not been materially modified since the remarkable renaissance of the French school of Bichat, Corvisart, Laennec, and Louis. The X-ray had been discovered by Röntgen in 1895, but roentgenology was in swaddling clothes in the early twentieth century. Indeed, two pioneers in roentgenology from Philadelphia—Leonard and Kassabian—had the fatal marks of their exposure when we were medical students. Our laboratory support was defined by the routine urinalysis, hemogram, and examinations of the secretions and excretions. Cytology and bacteriology played their appropriate roles, but the laboratory still served in a purely supportive role. Although surgical pathology had made material advances by the 90s, the diagnostic biopsy was still the exception.

EARLY TRAINING

The standards of medical practice commonly reflect the level of education of a given time. For perspective, the origins and the course of medical training in the New World must be explored. In colonial days, medical care for the settlers scattered on the Eastern seaboard was desultory and precarious. Preceptorial training under the trying conditions of the apprentice or house pupil status afforded the only door to the practice of medicine for aspiring young men until 1765. At the commencement of the College of Philadelphia that year, John Morgan, a native of the city and a graduate of Edinburgh, gave his classical "Discourse upon the Institution of Medical Schools in America." Its lofty principles and ambitious prospects were not to be realized for many generations, but he was named professor of medicine. Shortly thereafter, William Shippen, Jr., also a graduate of Edinburgh, was elected professor of anatomy and surgery. One of the new medical school's Scottish hallmarks was the institution of clinical instruction at Pennsylvania Hospital under Thomas Bond, who said: "(The student) must join Examples with Study, before he can be sufficiently qualified to prescribe for the sick, for Language and Books alone can never give him Adequate Ideas of Diseases and the best methods of Treating them. . . . There the Clinical professor comes in to the Aid of Speculation and demonstrates the Truth of the Theory by Facts . . . he meets his pupils at stated times in the Hospital, and when a case presents adapted to his purpose, he asks all those Questions which lead to a certain knowledge of the Disease and Parts Affected; and if the Disease baffles the power of the Art and the Patient falls a Sacrifice to it, he then brings his Knowledge to the Test, and fixes Honour or discredit on his Reputation by exposing all the Morbid parts to view and Demonstrates by what means it produced Death, and if perchance he finds something unexpected, which betrays an Error in judgment, he like a great and good man immediately acknowledges the mistake, and, for the benefit of survivors, points out other methods by which it might have been more happily treated."

The initiative of Philadelphia was promptly followed by New York. In 1768, King's College established a medical school that, faring the fortunes of war and certain local dissensions, ultimately became the College of Physicians and Surgeons of Columbia University. Medicine was offered at Harvard in 1783, but its real fruition awaited the movement to Boston in 1810. In 1796, medical courses were first conducted at Dartmouth. The nineteenth century was marked by an astonishing wave of new medical schools—their numbers were prodigious and their locations unpredictable. From 1810 to 1840 there were 26 new medical schools in this country, 47 were added from 1840 to 1876, and 114 originated between 1876 and 1890. In Missouri alone there were listed at one time or other 42 chartered medical schools! In the westward course of the tidal wave that was in many instances marked by brazen cupidity and flaunted morality, several institutions stand apart. At Lexington, Ky., Transylvania University made an auspicious beginning in medical education (1817), but contentious personalities and local dissension closed its doors. Cincinnati (1820 to 1908) and Louisville (1837) had areas of great strength at various periods, but the early exploitation of their educational advantage was sacrificed to petty bickering and insignificant personal differences. In the Middle West, Daniel Brainard led the way to the formation of Rush Medical College in 1837. Aside from the flagrant diploma mills conducted without thought of the standards of education, other institutions were ostensibly set up for the purpose of legalizing human dissection, such as those at Evansville, Ind.; Freeport and Rockford, Ill.; and LaCrosse and Madison, Wisc.

By the end of the eighteenth century, it is estimated that the medical schools of the country had graduated only 250 physicians. Several times this number had attended some courses in the medical schools. At this time, there were approximately 8,600 practitioners in the United States and, although an appreciable number had had the advantage of foreign education, the majority were the product of the preceptor system. In this relation it should be remembered that William Beaumont followed this informal pattern of training for two years and never attended the sessions of a medical school.

With due attention to the limitations of transportation, forty-five years later Davis justified the earlier relative weights of the preceptorship and the instruction in the medical schools as an expedient of time and substance. He concluded: "The idea of the founders of medical schools, both in Great Britain and in this country, was to make them supplement, but not supersede the work of the preceptor and the medical apprentice." However, by this time too frequently the preceptorship had fallen to the low estate of a mere registry.

MEDICAL SCHOOL IMPROVEMENTS

Whatever may have been the contributing factors, overcrowded with the cheap product of woefully incompetent instruction, American medicine became a national problem. The American Medical Association was the natural outgrowth of this concern. Convening under Nathaniel Chapman in 1847, this constituted body urged increased entrance requirements and standard two-year curricula for the medical schools. Pennsylvania and Columbia extended their annual sessions from sixteen to twenty weeks. Although supplemental private courses were offered between the regular sessions, the subject matter of that period was so limited that, in many instances, the lectures of the second year duplicated those of the first. The first departure from this conventional plan came from the Middle West under the guiding hand of Nathan S. Davis, who broke with Brainard of Rush on this issue. With the establishment of the Chicago Medical College (later to become Northwestern) in 1859, a carefully graded three-year course was offered. Its junior, middle, and senior courses represented a logical adaptation of progressive academic instruction. Twelve years later, Harvard accepted this principle and Syracuse followed suit. Beginning with the opening of the Johns Hopkins University Medical School in 1893 and Harvard's announcement in 1901, the requirements for admission to medical schools included certain levels of collegiate credits.

Into this sea of medical unrest the University of Minnesota College of Medical Sciences (under other names) was plunged. Of the state-supported medical schools of the Middle West, Ohio State (1847), Michigan (1850), and Iowa (1870) anticipated Minnesota. Pres. William Watts Folwell, famous author of the Minnesota Plan (1870), successfully thwarted efforts to stampede the regents of the university into ill-conceived plans for a medical school. However, a licensing board for physicians, divorced from teachers of medicine, was authorized. By the selection of its members from a panel nominated by the university, the state was placed in an enviable position for the control of medical practice. A member of this Board, Dr. Perry Millard of Stillwater, played a leading role in the resolution of the problems of the establishment of medical education in the university. Not only did he initiate negotiations, but by personal financial support he was responsible for the ultimate amalgamation of four inadequate medical schools—the Minnesota Hospital College of Medicine, Saint Paul Medical College, Minneapolis College of Homeopathy, and Minneapolis College of Physicians and Surgeons—as the University of Minnesota College of Medicine (1888). Because of inadequate facilities, the movement to the University campus was deferred several years.

The birth date of the University of Minnesota College of Medicine found medical education in the United States at its lowest ebb. By general agreement, a careful study of the situation was long overdue. To this herculean task, Abraham Flexner, with the support of the Carnegie Foundation for the Advancement of Teaching, was called. Flexner encouraged the physical or geographic association of the preclinical and clinical departments of the medical school. His arbitrary listing of the elements of the preclinical and the clinical curricula was to have an immediate impact on medical education and its repercussions are felt to the present time. The weakness of the large clinics and amphitheaters, as well as many administrative details, fell under his critical notice. The prospect of full-time appointments to major clinical posts, while remote, still offered much promise for the future. In this respect Frank Billings had anticipated Flexner. In the president's address to the American Medical Association in 1903, he advocated the full-time system with the reservation that there should be two types of representation in the clinical areas, namely, the full-time academic and the "clinical teachers who are in private practice."

Minnesota fared well at Flexner's hands. In his objective survey of May 1909, he described the laboratories as excellent, exceedingly attractive, and well organized in all scientific branches. The objective of full-time chiefs of the major services was applauded. Further, the prospect of a teaching hospital under university control had been strengthened by the provision of financial support that would assure appropriate staffing. Possibly another detail that attracted Flexner's attention was the annual budget of $71,336 for the College of Medicine at a time when 56 other medical schools operated on annual allotments of less than $10,000!

Obviously the season was ripe for the reform of medical education and practice in the United States. The fate of the less adequate medical schools was foreordained. Although the Flexner report had neither legal nor legislative sanction, public sentiment and professional conscience welcomed its revelation of glaring abuses and rank deficiencies. Its stark candor afforded no refuge for the most callous offenders. Forthwith the number of medical schools was reduced from 155 to 85. Among the survivors, a wholesome spirit of self-searching scrutiny vastly improved the content and the quality of medical curricula.

DEVELOPMENTS IN PHYSIOLOGY

Morbid anatomy and its relation to the disease expressions dominated clinical medicine until Virchow's principles carried medical thought to the cellular level. With the advent of microbiology, the etiologic diagnosis took precedence, and medicine experienced one of its most exciting phases as one after another causal factor was disclosed. Not infrequently, such discoveries were tantamount to the evolution of a protective or therapeutic biological agent to combat the disease. The spirochaeta pallida was discovered by Schaudinn in 1905. The serologic test for syphilis followed the next year.

From the nineteenth century emphasis on pathology and, latterly, bacteriology in clinical thought and practice, we passed almost imperceptibly into an appreciation of the important place of physiology and physiological chemistry in health and disease. Without loss of interest in the etiologic factors and their effects, increasing attention is paid to the changes in function and chemical reactions incident to disease. With the scientific advances in concept and methodology, such determinations have been transferred from the laboratory to the bedside at a breathless pace. To the elucidation of physiologic and chemical principles have come technological advances undreamed of a generation past. To cite an isolated example, serum proteins are characterized in many manners. In addition to the common biochemical tests, chromatography, electrophoresis, serology, immunochemistry, and ultracentrifugation may be invoked. Several radioisotopes have lent themselves admirably to the physiological and metabolic studies as tracers to establish the localization and the concentration of certain elements. Transferred to the clinical field, with the limitations imposed by their respective half-lives, these tagged elements have assumed an important role in diagnosis and therapy. Electron microscopy has opened an entirely new vista of normal and abnormal histology. With its wonders of magnification, chromosomes, microsomes, foot and brush processes, and a host of other details assume a reality that is lost to the familiar objects of light microscopy. Image amplification and cineroentgenography have greatly extended the range of diagnostic roentgenology. At an earlier stage, urography had revolutionized the study of the genitourinary tract. Cardiac catheterization with pressure and gas determinations, indicator dilution studies, and cineangiocardiography have brought a remarkable degree of objectivity to the field of cardiovascular disorders. Certainly the more exact definition of hemodynamic forces contributes inestimably to the assurance of successful cardiovascular surgery. This field of exciting proportions has been rendered accessible not alone by such physiological advances but by technological achievements such as extracorporeal circulation.

Cytogenetics is playing an ever increasing role in the understanding of human disorders. Familial and hereditary diseases have been the natural targets of such studies. Inborn errors of metabolism have been so related. Phenylketonuria, with the attendant mental deficiency, has followed this pattern. Aberrations of the Philadelphia chromosome (XXI) are associated with chronic myelocytic leukemia, and the absence of this fault has proved a sound basis for the exclusion of the leukemoid reaction. Most fruitful have been the explanations of certain hemoglobinopathies on genetic backgrounds. The breaking of the code of the double helix of deoxyribonucleic acid (DNA) and the appreciation of the messenger function of ribonucleic acid (RNA) have afforded a logical approach to the origin of life. Transplantation of tissue and organ has been a coveted objective of surgery for generations. The prospect of its more regular achievement has been greatly enhanced by the elucidation of the basic mechanism of rejection reactions and the development of methods for their control. Immunochemistry offers the logical approach. With overlapping into the field of microbiology, the thymus gland and the lymphocyte have assumed renewed importance as the sources of clones of immunologically competent cells. The introduction of a simple test, such as fluorescein staining, has added a new parameter to the studies of immune reactions. The diagnostic biopsy had won its place in the clinic by the early days of the twentieth century. Histochemistry in the broader sense is a relative newcomer. Enzyme chemistry has played a prominent role in the advancement of medical knowledge. Its manifest operations in the digestive processes and elsewhere are apparent. The vital functions of enzymes in oxidation, phosphorylation, decarboxilation, and countless other directions are well understood. Less appreciated may be their essentiality in the transport of electrolytes or other solutes across biologic membranes.

AUTOMATION

The application of automation to medicine is already extensive and there is much more in sight. After fighting a long rearguard action against random probing by expansive laboratory studies to derive a diagnosis, evidence is accumulating that batteries of 12 to 18 chemical determinations can be made rapidly and accurately by automatic analyzers on small specimens at a saving over conventional studies on highly selective materials. There is thus promise of a "chemical fingerprint" (Godber). The economy, comprehensiveness, and occasional serendipidous finding by this approach many eventually prevail over the psychological reservations. The Coulter counter has largely replaced the hemocytometer. The mechanical offices of the clinic offer an open invitation to electronics. Monitoring of vital signs by electronic means is an accepted procedure in modern surgeries and recovery rooms. The transmission of vital signs, blood pressure determinations, electrocardiograms, and electroencephalograms over great distances by telemetry is a marvelous demonstration of the advanced stage of this development. The cardiac pacemaker is a natural application of the transistor for the rhythmic stimulation of the myocardium in atrioventricular heart block with Adams-Stokes manifestations.

Automatic data processing has invaded many fields of human endeavor. Its inroads into medicine were first in the laboratory and then in administrative fields, where repetitive "hard" data invited the speed and accuracy of the computer. The ability of the machine to receive, store, and deliver information on command much more effectively than the unaided human mind is indisputable. Perceptive programming and accurate input will assure satisfactory retrieval. Already by appropriate techniques of transfer of the electrocardiographic signals to the computer, an accuracy of approximately 95% in reading has been attained. Automatic data processing will eventually revolutionize history taking, hospital records, patient control, and the dispensing of drugs. At some future time, the automation of these procedures will pass from the individual institution to the community, then to the region, and to the nation so that the experience of the entire medical profession will supplant that of the individual practitioner. Already its principles are being applied in record linkage on a regional basis in Great Britain (Acheson).

PHARMACOLOGY

Therapeutic nihilism was abroad seventy-five years ago. Quinine, opium, and digitalis were the trusted sheet anchors of therapy. Mercury and the iodides held a limited but respected place. In general, galenical drugs prevailed. Vaccination against smallpox was the only widely accepted biological prophylactic measure in 1890 (von Behring). Diphtheria antitoxin was discovered that year. Polytherapy on an empiric basis was the rule. With man's eternal interest in drugs, the advances in pharmacology and therapeutics on sound scientific grounds have attracted widespread notice. Assuredly, they have radically altered the practice of medicine. But in an evaluation of the total picture, the contribution of hygienic and preventive measures must be given due weight. Under their influence, diphtheria and the exanthems have shrunken in importance. Typhoid fever is now deemed a reflection on the good name of a community. Pneumococcus lobar pneumonia, a commonplace in my student days, is now rarely seen in its classical form in our major hospitals. Tuberculosis has lost its awesome significance. Most striking among the contributions of preventive medicine has been the virtual disappearance of tuberculous cervical lymphadenitis, tabes mesenterica, and tuberculosis of the bones and joints upon the eradication of bovine tuberculosis in this country.

Turning to the therapeutic advances of the past seventy-five years, one must exercise Procrustean prerogatives. One great breakthrough was discovery of salvarsan (Ehrlich and Hata, 1910). For the first time, the principle of therapia sterilisans magna was vindicated in the affected patient. Syphilis was rendered vulnerable to therapeutic control, but human frailty has denied its eradication. There followed the frenetic and frustrating quest for analogous agents to combat bacterial infections. The efficacy of sulfonamides (Domagk, prontosil, 1935) brought a new concept and renewed hope to a fallow field. Sulfapyridine (Whitby, 1958) proved especially effective in pneumococcus infections. Scarcely had these agents gained a foothold when new and unanticipated developments opened the virgin field of antimicrobial therapy. With a sustained interest in lysozymes, Fleming isolated penicillin in 1928, but its application to human ills awaited the catalytic force of World War II and the diligence of the Oxford group (Florey et al.) for its ultimate exploitation. Of the host of antimicrobial agents that has since been brought out, streptomycin (Waksman, 1944) deserves a special notice. To its virtues we owe the first aggressive defense against tuberculosis. Special tribute is due John R. Barnwell and Arthur M. Walker for their design of the cooperative chemotherapy study of the Armed Forces and the Veterans Administration that firmly established the efficacy of streptomycin. Their approach will serve as a model for all future mass therapeutic trials. Inviting as is the widening field of antimicrobial therapy, it must be dismissed with several broad generalizations. In certain respects, these potent agents have been two-edged swords. Resistant strains of microorganisms have emerged. Sensitivity to these potent remedies has given not only serious and even fatal reactions but has denied their availability to patients sorely in need of their support. In their indiscriminate use, the profession must assume its share of the responsibility for this situation. In a more subtle fashion, the advent of the antimicrobial agents has altered the mode of infectious diseases. By the destruction of common bacterial forms, these marvelous elements have created a striking biologic imbalance. This dislocation is evinced by the ascendency and pathogenicity of unusual bacteria, fungi, and viruses. Most recently, idoxuridine (IDU), an analogue of thymidine, offers promise in combating certain viruses.

Substitution therapy for hypothyroidism was initiated by Murray in 1891. Thyroxin was isolated by Kendall in 1914. Osler commented on the miraculous relief of the asthmatic seizure by epinephrine (Abel, 1898). Parallel experiences attended the first injections of insulin (Banting, Best, and Macleod, 1922). The impact of this discovery of the basic understanding and management of diabetes mellitus cannot be exaggerated. Interesting, however, was the early revelation of the unanticipated complexity of the problem. Houssay's experiments from 1921 to 1930 demonstrated the interdependence of the hypophysis and the islands of Langerhans. Continuing to the present time, advances in the knowledge of this involved subject emphasize this circumstance. By immunoassay, Berson and Yalow (1959-60) have determined normal or increased levels of serum insulin in patients who developed diabetes mellitus at maturity. And so the exciting developments in endocrinology could be vastly expanded.

Hematinic agents were limited seventy-five years ago. Various forms of iron occupied a prominent place. With the experiences of World War I, renewed interest came to blood transfusions and their substitutes in the control of traumatic shock. Blood grouping gave security to the procedure and in the interwar period, transfusions took their proper place in modern practice. However, these measures afforded no sustained support for patients with pernicious anemia. With the fundamental work of Whipple and Robscheit-Robbins in 1925 came the evidence of the unusual virtue of liver in the regeneration of hemoglobin in standard anemic dogs. With characteristic alacrity and direction, Minot and Murphy (1926) successfully applied the principle to patients suffering from pernicious anemia. To Castle belongs the credit for elucidation of the interaction of the intrinsic and extrinsic factors by his classical experiments in 1928. The impetus of these contributions revitalized this aspect of medicine to culminate in the definition of the role of vitamin B_{12} (cyanocobalamine). Its force continues with unabated productivity. In spite of the promise of virology in explanation of some forms of leukemia in animals (Gross et al.), practically all therapeutic approaches are directed toward destructive or antimetabolic agents against the neoplastic process. Without minimizing the importance of this direction of attack, further progress may be anticipated through new and basic principles that hopefully might help solve the secrets of neoplasia in general.

The discovery of the adrenal steroids and the definition of the pituitary-adrenal axis have had a profound effect on medical thought and practice. Limiting the discussion to the adrenal cortical extract (Reichstein, 1936; Kendall and Hench, 1937), unquestionably the availability of cortisone gave medicine the most potent agent it has ever possessed. Its powers have operated both to the benefit and to the detriment of the subject, but the balance is strongly on the credit side of the ledger. In many instances, its actions have served to solve physiologic questions.

The tranquilizing agents have enjoyed wide and uncontrolled usage. Their beneficial action is unquestioned, but classical modern methods of control study are difficult. Certainly, they have rendered patients with mental illness more accessible to recognized forms of therapy, and the tide of bed occupancy for such patients is at last ebbing.

IMPACT OF SPECIALIZATION

Isolated as these cited instances of scientific advances are, with a vast number of other aspects, both basic and clinical, their burgeoning force toward specialization is inescapable. Not only is it impossible for the superior mind to grasp all medical progress but its possessor is fortunate to keep abreast of even a limited segment of medicine. Nevertheless, in this period of specialization, medicine must perforce take a long look at its proper place in society of the future. Studies have indicated the need for more physicians. Medical educators are frantically attempting to close the gap by increasing the students in existing schools and the number of schools. Physical limitations are encountered in both directions, but promises of substantial relief have been made. An even more serious obstacle to the successful assault on this problem is the difficulty in the recruitment of the medical staff. A recent survey disclosed over 900 funded vacancies in our medical faculties. Salaries are scarcely competitive with opportunities elsewhere, but a more telling argument is not difficult to find. In the presence of abundant money for research, often from federal sources, the young man of promise is hard pressed for reasons to accept a teaching assignment where academic advancement is less rapid and less assured. We must breed a generation of well-motivated young physicians for whom teaching is not a second-rate academic prospect—and make it stick.

In self-protection, medicine must seriously contemplate its proper place in society. No longer can we maintain our proud isolationism. The stepping stones, on which the revered physician of the past precariously made his individual way, are being swept from under his feet. More and more he has come to realize that he is a member of society—a servant, not a master. This statement is made without a feeling of denigration, but with a realization that health is the natural birthright of every human being. Medicine is the keystone, but not the entire arch, of the health team and every physician must be a member. No longer may he feel himself the sole custodian of this precious commodity, to which so many contribute in modern society. Indeed, to this protective circle nursing was first admitted. Dietetics was a natural partner. With rehabilitation, the early attention was directed to physiotherapy and occupational therapy. With due thought to the mental aspects of health and disease, clinical psychology joined the ranks. Social service had earned its place when due thought was given to the environmental and other social forces that operated on the person under study.

From a period when medicine was practiced in the home and office, we have witnessed a gravitation to the hospital. Urbanization and transportation have been active factors in this movement. Under voluntary insurance plans and federal support, this tendency will grow. Specialization requires the highly refined instrumentation and equipment that only a hospital can afford. These circumstances combine to encourage associate and group practice, but they do not deny the advantage of independent practice—with appropriate support.

Indeed, the need for the family counselor was never greater. With proper training he can give satisfactory care for 75% of the common ills and will relieve the highly specialized psychiatrist of 50% of his misdirected clientele. Obviously such a practitioner may function in the group or associate capacity as well as individually. This well-motivated practitioner may siphon an appreciable number of patients from our overloaded hospitals for appropriate attention in the office and home. Certainly, in the future as in the past, the family counselor will more distinctly reflect the image of medicine to the public than any of his more sequestered professional brothers in the larger medical centers.

SUMMARY

As one would anticipate, radical changes have occurred in the transition from the horse and buggy medicine to the space era. The empiricism that still marked the 90s has given way to the scientific approach in the laboratory, clinic, and sickroom. The modern physician is capable of infinitely more exact practice than his grandfather. Therapeutic advances have vastly improved his care of patients. The surgical approaches to intracranial lesions, diseases of the lung, and disorders of the heart and vessels are essentially all developments of this period. Truly there are no secret hiding places that escape the modern surgeon. Specialization is basically a product of this period through the vast growth of medical knowledge. The manner of practice shows a steady movement toward the hospital. Although abundantly evident at this time, automation and mechanization will be increasingly utilized in medicine in the future. Let us consider: seventy-five years from now, some essayist will reflect on the backward state of the science and the art of medicine in 1966. Certainly, ever broader, brighter vistas are still ahead.

Cultural and Environmental Changes Affecting Health and Medicine

HUDSON HOAGLAND

Shrewsbury, Massachusetts

Over the last century, since Darwin's *Origin of Species* in 1859, we have learned that the survival of living organisms and their evolution by natural selection are dependent upon their ability to adapt to changing conditions in their environments. For each species here today, it is believed that thousands have become extinct because of failures to adjust to environmental changes.

It was also just a century ago that the French physiologist, Claude Bernard, pronounced his famous dictum that "the fixity of the internal environment is the essential condition for a free life." By this, he meant that fitness for survival involves freedom from the vicissitudes of a changing external environment and that to realize this freedom physiological mechanisms are required to regulate the stability of the chemical and physical properties of fluids bathing living cells so as to maintain, within limits, the steady-state chemical processes that constitute the life of the cells. Relative constancy of the cellular environment is necessary for their continuous food supply and their metabolism and for removal of waste products. Those animals able to maintain relative constancy of body temperature, electrolytes including acidity, and other chemical constituents of blood, lymph, and cerebrospinal fluid are freed from many vicissitudes of changing external variables and are thus better able to adapt to change. Also, I suggest that freedom may be considered as the ability to change behavior appropriately with circumstances. In the course of evolution, Dobzhansky has pointed out that the extinction of species may be a consequence of their becoming rigidly and irrevocably adapted to environments that do not endure.

Studies of mechanisms for the regulation of the internal environment, chemical buffer systems of the blood, endocrine systems, autonomic and neuromuscular systems regulating blood pressure, heart rate, respiration, and mechanisms of digestion and elimination have, for a century, been major fields of physiological research. In the first half of this century, the studies of the late Walter B. Cannon and his associates analyzed homeostasis of the internal environment in terms of the role of autonomic nervous mechanisms and of the hormone adrenalin from the adrenal medulla that mimics or boosts the action of the sympathetic nervous system. These mechanisms have been shown to regulate the internal environment in the face of marked changes including vigorous exercise and actions involved in fighting and escaping from danger and their accompanying emotions of anger and fear.

In recent decades, our knowledge of how we meet daily environmental stresses has further advanced. Situations calling for flight or fight, with their concomitant emotions, are stressful. But, inhibiting our aggressions or desires to flee from unpleasant daily situations—political, domestic, or occupational—may produce chronic anxiety states. Also, psychological stress may result from the intensification of our instinctual drives of sex and aggression and the control of these drives to meet the demands of society. Such stresses, often chronic, contribute to the production of psychosomatic disturbances in the form of neuroses, hypertension, atherosclerosis, arthritis, skin disorders, asthma, and allergies. The balancing of one's needs and drives in terms of socially demanded inhibitions produces stresses of this sort. The apparently same external stress situation may have quite different psychological significance for different people in terms of their past experiences, so that attempts to objectify and standardize such stresses meet with difficulty. Investigators have reported marked fluctuations of various disease states with stresses over an individual's life-span. Remarkable correlations are found of both mild ailments and disabling diseases with such life stresses as un-

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HUDSON HOAGLAND *is with the Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts.*

happy marriage or divorce, anxiety over loss of job or threat of its loss, anxiety over family illnesses, family quarrels, and lawsuits.

The physiologist has a variety of measures of how stress may disturb the body's regulation of the internal environment of its tissues. Blood and urinary measurements of certain endocrine systems brought into play by stress are particularly useful response indexes, physiological measures of action of the sympathetic nervous system and quantitative analyses of blood and urinary adrenalin and noradrenalin—a neurohumor primarily released at synapses and nerve endings of the sympathetic nervous system—reflecting defense responses to acute stress. Blood and urine measurements of the steroid hormones from the adrenal cortex and their metabolites have been used more widely than any other indexes in recent years in studies of stress responses. The adrenal cortex is activated by the pituitary adrenocorticotrophic hormone (ACTH), which, in turn, is released in increased amounts by action of the hypothalamus following bodily injury or threats as well as a variety of emotionally laden stresses. The adrenocortical hormones have ubiquitous actions on many tissues involved in response to stress in the maintenance of homeostasis of the internal environment.

Hans Selye, over the past thirty years, has developed the concept of the general adaptation syndrome, which he defines as the characteristic emergency reaction or general response to stress. It develops through three stages: [1] the alarm reaction, in which adaptation to the stress is attempted, [2] the stage of resistance, in which adaptation of bodily mechanisms is optimal, and [3] the stage of exhaustion, in which adaptation of homeostatic mechanisms fail. These various phases of the general adaptation syndrome may be studied in terms of the type of changes in constituents of body fluids, especially those involving activity of the adrenal cortex. Indexes of adrenocortical function in animals may include determinations, before and after stress, of adrenal size, adrenal ascorbic acid, and adrenal cholesterol, as well as adrenocortical hormones and their metabolites in blood and urine. Selye has concluded that many diseases are primarily a result of failure of the bodily mechanisms of adaptation to meet chronic stress situation adequately. While the matter is controversial, he considers that disturbed patterns of endocrine secretion following the prolonged application of stressors may result in various chronic diseases and so be caused by aberrant homeostasis, and he thus speaks of the diseases of adaptation resulting from prolonged stress with accompanying shifts in the chemical nature of the pattern of steroid hormones released by the adrenal cortex.

In our sedentary, urban society, many regulatory mechanisms that evolved by natural selection to cope with life in the wild find themselves called upon inappropriately, with resulting psychosomatic ailments as a consequence. In this connection, Curt P. Richter has made interesting comparisons between wild rats and those domesticated, that is, reared in laboratories over many generations of inbreeding. As a result of selection by breeders for tameness and other qualities for laboratory use, the domesticated rat differs in many ways from contemporary wild members of his species and from his wild ancestors. The wild rat is much more aggressive, tough, and resourceful and has marked ability to meet stress and resist fatigue, compared to its domesticated relatives. In the domestic rat, the adrenals are much smaller than in the wild rat and the thyroid is less active. The gonads, responsible for sex activity and fertility, develop earlier and produce many more offspring than in the wild rat. The brain is smaller and the animals are more susceptible to various types of fits. Generations of selection for domesticity has produced an animal less able to meet and survive in a natural environment.

Many diseases have a predisposing genetic basis. These include schizophrenia, cardiovascular disease, gout, some epilepsies, diabetes, and perhaps some cancers. There are other diseases of highly specific genetic origin such as phenylketonuria, sickle-cell anemia, and hemophilia. Alarm has been expressed by some geneticists over selective factors at work through the humanitarian practices of our culture of keeping people with such genetic defects alive and enabling them to reproduce and so add to man's load of harmful genes. Such defective genes, without support from modern medicine, would die out because of the disadvantages they produce for their carriers. But bearers of defective genes are often highly desirable citizens, like the diabetics, many of whom, before the advent of insulin in the 1920s, would not have lived to have offspring.

The distinguished geneticist H. J. Muller has argued that some hundreds of generations hence much of our daily occupation will be in producing and using medicines and prosthetic devices to keep ourselves functioning. But intelligence itself may fail as a result of an increasing burden of crippling genes before we reach this sorry state.

From the foregoing discussion, disease may be regarded as the result of inadequacies of adaptation to environmental changes. René J. Dubos[1] has defined health as "an expression of fitness to the various factors of the total environment and fitness is achieved through countless genotypic and phenotypic adaptations to these factors." There is a general belief held by both professional workers as well as laymen that all we need is more and more biomedical research to relieve man of his burden of diseases and usher in a sort of medical utopia. Dubos has criticized this optimistic view since the relief of one disease, or group of diseases, leaves us the victim of others and there seems to be no escape from the shifting of human misery and the causes of death from one category of disease to another with medical progress.

Thus, there have been remarkable advances in the control of infectious diseases over the last century beginning with Pasteur, with later developments of microbiology, parasitology, and immunology. Control of such diseases as typhus, malaria, plague, typhoid, pneumonia, childbed fever, and smallpox has enhanced life expectancy but left us increasingly the victims of destructive metabolic disorders characteristic of an aging population such as arthritis, emphysema, cancer, and cardiovascular diseases. The American Heart Association, in its drive for support, has pointed out that half of us may expect to die of cardiovascular ailments, and the American Cancer Society has said that a seventh of us will probably die of cancer. But of course all of us will die. Certainly, this is no reason to discontinue to search intensively for the cause and cure of both of these diseases, even at the risk of leaping from the frying pan into the fire at still older average age levels. Medical advances have markedly increased life expectancy although they have not lengthened the human lifespan as such. Drugs, analgesics, and anesthetics have also alleviated suffering from crippling disorders. But, on the subject of medical utopias, Dubos has written:

"A perfect policy of public health could be conceived for colonies of social ants or bees, whose habits have become stabilized by instincts. Likewise, it would be possible to devise for a herd of cows an ideal system of husbandry with the proper combination of stables and pastures. But unless men become robots, their behavior and environment fully controllable and predictable, no formula can ever give them permanently the health and happiness symbolized by the contented cow. Free men will develop new urges, and these will give rise to new habits and new problems, which will require ever new solutions. New environmental factors are introduced by technological innovations, by the constant flux of tastes, habits and mores, and by the profound disturbances that culture and ethics exert on the normal play of biological processes. It is because of this instability of the physical and social environment that the pattern of disease changes with each phase of civilization and that medical research and medical services cannot be self-limiting. Science provides methods of control for the problems inherited from past generations, but it cannot prepare solutions for the specific problems of tomorrow because it does not know what these problems will be. Physicians and public health officials, like soldiers, are always equipped to fight the last war."

The role of the environment in determining health and mortality is of course highly important. People in the tropics suffer from malaria; workers from rock quarries suffer from silicosis. Laboratory workers may be exposed to the fumes of organic chemicals damaging blood-forming organs, and the industrial use of nuclear energy presents new health hazards, as do the pollutions of air and water supplies by industry and of food by insecticides. While city dwellers are not exposed to various parasitic diseases such as hookworm that enter the body through bare feet, they may continually inhale atmospheric pollutants that in susceptible persons facilitate the development of chronic bronchitis, emphysema, and possibly lung cancer. Our exposure to Madison Avenue selling pressures, an integral part of our culture, assists in the widespread use of attractively packaged carcinogens in the form of cigarettes, and our people, supplied with an overabundance of fatty foods, have an exceptionally high incidence of coronary accidents and strokes from deposition of fatty materials in critical blood vessels in heart and brain so that the vessels break or become occluded with clots. Oriental peoples subsisting on rice and other peoples on low-calorie diets lacking animal fats show marked freedom from atherosclerosis, the major killer of us opulent Americans. The stone-culture aborigines of Australia are remarkably free from most disease. One is reminded of Richter's comparison of domesticated and wild rats, although the comparison may be entirely fortuitous as to mechanisms.

For the control of infectious diseases, the advent of antibiotics was, of course, a major advance, but our way of doing things has resulted in their use promiscuously for disorders that they cannot relieve, such as viral infections, often on the chance that a susceptible bacterium may be lurking in the background, at least as a secondary infection. This has resulted in a marked decline in effectiveness of penicillin and other antibiotics as bacteria develop resistant mutants. Antibiotic prophylaxis directed particularly against meningococcal and beta-hemolitic streptococcal infections, while successfully preventing these diseases, has nonetheless developed drug-resistant mutants of the pathogenic organisms. Penicillin has been used for the treatment of gonorrhea for the past twenty years, but the disease has increased rapidly over the last ten years due to the fact that the gonococcus developed resistant mutants. H. Koprowski considers that some of this increase has resulted from the knowledge of the availability of what was an effective therapeutic antibiotic. This may have enhanced sexual promiscuity and so facilitated a wider spread of the disease. The development of drug-resistant mutants of staphylococcus in hospitals is a common observation, as is the development of mutant forms of insects resistant to DDT. These effects are typical of many pathogenic organisms so that one must run as fast as one can to develop new antibiotics to keep ahead of the mutating pathogens.

Constitutional factors involving resistance to disease may involve both genes and environment. Recently, Frederick Epstein and his collaborators reported a cardiovascular study of 10,000 residents of Tecumseh, Michigan. They investigated four factors associated with cardiovascular disease. These are relative weight, systolic blood pressure, blood sugar, and blood cholesterol. They found that closely related members of the same family strikingly resemble each other in these four variables. This further supports the view of a genetic factor involved in cardiovascular disease based on earlier data indicating a tendency for coronary accidents and strokes to run in families. These observers also reported, however, that environment plays an important role. Thus, reduction of calories—especially fat—in the diet, also changes in modes of living so as to reduce stress, and other environmental factors can favorably modify these physiological indexes and reduce the frequency of cardiovascular accidents despite predisposing genetic factors. This kind of interplay between genes and environment in health and disease is the rule rather than the exception, and sickle-cell anemia is a case in point. This anemia is characterized by the presence of sickle-shaped red blood cells which are very inefficient carriers of oxygen. The sickling is due to a particular gene which slightly modifies the order of arrangements of an amino acid in the hemoglobin molecules which are the oxygen transporting units of the red blood cell. This disease is found in residents of the tropics, more particularly in Negroes in Africa living in malaria-infested zones. It has been found that offspring receiving the deficient gene from both parents generally fail to live to maturity. However, the inheritance of the sickle-cell anemia gene from one parent only, while debilitating in relation to oxygen-carrying capacity of the blood, is not fatal. Rather, it conveys upon its possessor, for reasons quite unknown, a resistance to malaria. Thus, the gene, lethal in double dose, has survival value for single-dose offspring living in malaria-infested areas. For this reason, this lethal gene instead of dying out has survived. When Negroes have come to America and settled in malaria-free zones, the disadvantage of the sickle-cell genes causes them to die out over a relatively few generations in the new environment.

POPULATIONS, CULTURES, AND MEDICINE

We have been considering aspects of how cultural and environmental changes affect health and medicine, and I would now like to discuss the converse of this, namely, the effect of changing conditions of health and medicine on cultural and environmental factors. The most outstanding example of this last is, of course, the population explosion resulting from declining death rates due to medical and public health advances. The impact of this on our culture and environment is marked and may become catastrophic.

It is indeed ironical that the humane practices of medicine and public health, dedicated to reducing physical suffering and prolonging healthful lives, should be the primary cause of a major social disease which is the unprecedented upsurge in populations. For a hundred years before World War II, following Pasteur and the development of bacteriology, European and North American population growth rates increased slowly as a result of the conquest of infectious diseases and improvement in public health practice. Thus, death rates were reduced and life expectancy was increased from 40 to 70 years since 1860. Since World War II, Western medicine has administered its highly sophisticated techniques in underdeveloped countries on a grand scale. Medical missionaries, using relatively inexpensive insecticides, antibiotics, inoculations, and vaccinations applied to masses of people, have drastically reduced death rates, leaving birth rates, always large, either unchanged or somewhat increased as a result of improvements in health and longevity. This beneficent process has greatly increased populations in the poverty-stricken countries of Asia, the Near East, Africa, and Latin America, which now contain 69% of the world's adults and, through marked decreases in infant mortality, 80% of its children. Population growth rate is the difference between birth rate and death rate. The basic ingredient of the world population explosion is, thus, lowered death rates, which it took European countries over a century to achieve and which are being approached in underdeveloped countries in a fifth to a tenth of the time. But large birth rates in these countries, which it took Europe sixty to seventy years to bring down to modern levels, show no sign of decline.

In some of the poorest countries, the population is increasing at the rate of over 3% per year, which will double it in less than twenty-three years. The world population as a whole is increasing at 2% per year, a rate which will double it in about thirty-five years. Nothing like this has ever happened before. It has taken roughly a million years of human development for us to reach a world population of 3 billion in 1960. It will require only another thirty-five years to double this to over six billion. It will double again to 12 billion in another thirty-five years and go on, not only with no sign of slowing in sight but actually with increasing rates of growth in many of the poorest countries. Oncoming generations of poverty-stricken, economically unproductive young people will increase the birth rate further as they come of age. Already, this generation in some countries is more illiterate than that of its parents and has fewer job opportunities. This is bad news in countries with rising expectations, which now contain two-thirds of the world's people, such as China, India, Pakistan, the United Arab Republic, and various Latin American countries where the average per capita income is less than $100 per year. It is also bad news for us in the opulent countries since these people will insist on a more equitable distribution of the world's goods, and a third world war of utter destruction is made increasingly likely by their discontent.

There are only two solutions to the social disease of world overpopulation. One is to increase death rates, and the other is to decrease birth rates. There is no other way. So far, we have manipulated death control by decreasing death rates and so are increasing the population. No one that I know of advocates reversing this process, although a nuclear war would certainly do so, and such a war is made increasingly likely by runaway populations of poverty-stricken, contentious, national groups and opportunist leaders. The alternative solution is, of course, birth control and family limitation on a rational basis. Man is the only animal that can deliberately direct and control his own evolution. It will be interesting to see which of these two variables, death rates or birth rates, he will utilize. It must be one or the other, or both, since a 2% growth rate will result in 1 sq. yd. of land area per person six hundred years hence, an obvious absurdity. No amount of scientific farming or other technological developments can be more than palliative and that for only another four or five generations.

Modern man alone among the animals fails automatically to control his populations. Most animals maintain their populations fairly level, subject to cyclic fluctuations, by remarkable automatic, instinctive methods of population control. Thus, in cultures of microorganisms—bacteria and yeasts—grown in a culture medium in glass vessels, the growth rate accelerates exponentially; but, as toxic metabolic byproducts, such as acids or alcohols, accumulate, the environment is changed, the growth rate declines, and the curve describing numbers of organisms as a function of time ultimately flattens off and becomes S-shaped.

Primitive human populations, when relatively isolated by geography or by cultural factors, also display S-shaped growth curves; in other words, the growth accelerates and then flattens out, the deceleration results from Malthusian brakes such as infectious diseases, war and famine, and sex taboos, marriage customs, and infanticide; or, more hopefully, it results from, as in the past, migration to other lands or, even rarely, from rational family planning through birth control. This last form of population control is unique to man. The motivation for family planning has generally been a desire of parents for better economic and educational advantages for small families and hope for their own and their children's upward social mobility. It is this factor that is primarily responsible for the small present growth rates of about a half of 1% in the most advanced industrial nations of Europe, rather than the Malthusian factors active in more primitive societies.

Some animal societies have remarkable mechanisms to regulate populations in relation to social environment. Thus, fruit flies, grown in a milk bottle, above certain population densities decrease their egg laying to an amount proportional to the number of flies present, even when plenty of food is kept available. Many investigations have been made of flour beetles. Below a fixed number of grams of flour per beetle, cannibalism occurs in some species, egg production drops off, and in one species crowding results in females' puncturing and destroying some of their eggs. The frequency of copulation also declines with crowding. There are some species of flour beetles with glands that produce a gas, the release of which is increased with crowding. This gas is lethal to larvae and acts as a beetle antaphrodisiac at high densities of beetle population. Flour contaminated with beetle excrement inhibits egg production of one species, and the mixing of this contaminated flour with fresh flour decreases the rate of population growth, which is entirely reversible in the presence of fresh flour. In these cases, the food supply is ample.

Among populations of mammals other than man, Darwin thought that food limitation and predators were the controlling factors in limiting populations of rabbits, lemmings, and other rodents as well as of deer, caribou, and other forms. While these may be important, the situation is not so simple. Thus, the snowshoe hare population of Minnesota has been studied extensively. These populations rise and fall through cycles of about ten years' duration. There is a period of buildup followed by a dying off. Why do these marked oscillations in numbers occur? It was observed that when the animals died off there was usually plenty of food—they had not starved. There were no evidences of an excessive number of predators. Furthermore, the bodies showed no sign that any specific epidemic had killed them. Postmortem examinations showed fatty degeneration and atrophy of the liver with a coincident striking decrease in sugar stored in the liver and low blood sugar preceding death. Many small hemorrhages and congestions of the adrenal glands, thyroid, kidneys, and brain were frequent findings. The hares often died in convulsive seizures with sudden onset and running and leaping movements. Others were typically lethargic and died in coma. The adrenal glands were enlarged in some cases and atrophied in others. There was evidence of liver disease, hypertension, atherosclerosis, and adrenal deterioration—signs typical of what one finds following prolonged stress producing overactivity of the pituitary-adrenal axis, that is, Selye's stress syndrome discussed above.

In studies of various rodents, including the hares, it has been found that accompanying the severe stress of winter crowding in burrows, there was much fighting among the males, sex drives were at a low ebb, the young were often eaten, and the females produced many premature births. Increased susceptibility to infections of all kinds was found, which is another byproduct of excessive production of adrenocortical hormones of the cortisone type. After the numbers of such a colony are depleted through the effects of stress, the colony then tends to build up again, going through repeated cycles of growth and decline.

Studies made of the crowding of animals in cages in the Philadelphia Zoo disclosed that in some species there was a tenfold increase in atherosclerosis under conditions of severe crowding, as well as many other symptoms characteristic of stress. John Christian of the Naval Medical Research Institute made population studies in relation to the crowding of mice. As a result, Christian[2] wrote: "We now have a working hypothesis for the die-off terminating a cycle. Exhaustion of the adreno-pituitary systems resulting from increased stresses inherent in a high population, especially in winter, plus the later winter demands of the reproductive system, due to increased light or other factors, precipitates population-wide death with the symptoms of adrenal insufficiency and hypoglycemic convulsions."

One of the most interesting studies has been made at the National Institutes of Health by John Calhoun who has studied effects of crowding on rats. He investigated colonies of rats kept in pens at critical levels of crowding and under these conditions observed high infant mortality, high abortion rates, and failures of mothers to build nests. The young were often scattered about and eaten. When the rats were examined, there was also evidence of the stress syndrome, and Calhoun has spoken, most appropriately, of what he calls "pathological togetherness."

To what extent may the stress syndrome be a limiting factor in reducing the growth rate of human populations? As far as I know, there are no adequate data on which to base an answer. Studies from a number of laboratories, including our own, have demonstrated that the human pituitary-adrenal system responds to stress in a way similar to that of other mammals. There is evidence that inmates of concentration camps experienced acute forms of the stress syndrome that probably accounted for many deaths. Concentration camps would be more appropriate sources of comparison to highly congested and confined animal populations than city slums, since in crowded cities even the very poor have some mobility. They can escape from their immediate congestion onto the streets and associate with other members of the population. The increased incidence of atherosclerosis and other cardiovascular pathology associated with urban living and its competitive stresses may also be enhanced by crowding, although direct evidence for this is lacking. In underdeveloped countries with high birth rates and recently lowered death rates, any possible increase in death rates occasioned by the stress syndrome would be statistically obliterated through the action of medical and public health measures that are enhancing life expectancies and would thus mask any smaller reduction in life expectancies from social stress.

Most animals from ants to man are gregarious and form social groups. V. C. Wynn-Edwards points out that by controlling a specific piece of ground a bird or other animal or group of animals controls its food supply on that range, and populations are not allowed to exceed its food productivity.

Population is controlled by the expulsion of low-ranking members of the group, by deaths from stress and from cannibalism, and by killing of the young. These are widespread accompaniments of crowding. Cannibalism produced by crowding is found in fish, crabs, spiders, and insect larvae of various types as well as in birds and mammals. Infanticide has been widely practiced by man—but usually for reasons other than population control—in classical Athens and Rome and in various countries of Europe, India, and China. However, in all animal cases investigated, the mortality from animal cannibalism and killing of the young is density dependent and ceases below a certain critical density, although for man other factors—religious and economic—may be involved in infanticide.

Modern man appears to lack the built-in restraints of animals. We overgraze our land, converting it to deserts. We have exterminated our passenger pigeons and nearly all our bison and sea turtles. Whales, the rhinoceros, southern fur seals, leopards, polar bears and Alaskan bears, mountain lions, and so on, are on the verge of extinction in the name of sport or because of commercial greed.

Wynn-Edwards has argued that primitive man, limited to the food he could get by hunting, had evolved a system for restricting his numbers by tribal traditions and taboos, such as prohibiting sexual intercourse for mothers while they were still nursing a baby, practicing compulsory abortion and infanticide, offering human sacrifices, conducting headhunting expeditions against rival tribes, and other quite unpleasant activities. Life was nasty, brutish, and short, and death rates and birth rates were high. These customs, consciously or not, kept the population density nicely balanced against the feeding capacity of the hunting range. Then, some eight thousand to ten thousand years ago, the agricultural revolution removed that limitation. There was no longer any reason to hold down the size of the tribe; on the contrary, power and wealth accrued to those tribes that allowed their populations to multiply and to develop farms, villages, and cities. Death rates from disease and war were still high and religious leaders exhorted their followers to fructify and multiply, not only to keep pace with the high death rates but to have soldiers to maintain their power structures. The old checks on population growth were gradually discarded and forgotten. The rate of reproduction became a matter of individual choice with fertility urged on by priest and ruler, and tribal or community control was lost.

Given opportunity for procreation and a low death rate from medical advances, the human population now shows a tendency to expand without limit. Lacking the built-in homeostatic systems that regulate the density of animal populations, man cannot look to any natural process to restrain his rapid growth. If the birth rate is to be slowed down, it must be by his own deliberate, applied efforts in the use of effective contraceptives, a field in which remarkable progress has been made, especially in the last decade.

The population explosion is one of several major crises brought on by rapid advances in science with which our traditional social concepts and institutions are inadequate to deal. The advent of nuclear weapons in 1945 with the Hiroshima bomb is another environmental change of catastrophic potential. Nuclear weapons have made obsolete national sovereignties as a way of giving security to citizens. Since all organisms must adapt to environmental changes or perish, history may record, if there should be any history after a third world war, that man became extinct because of his inability to adapt to a nuclear environment—his cerebral cortex, responsible for his unique position as the dominant animal, had, after all, turned out to have been a phylogenetic tumor.

Clearly, new ways of thinking about changes resulting from these great new developments are necessary. Medieval concepts of the nature of man cannot cope with the population problems, nor can nineteenth century concepts of nationalism protect us in the nuclear age. These are the great problems of psychosocial evolution on which our very survival depends and their solutions constitute the major challenges of our time.

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The Mounting Costs of Medical Care: Fundamental Issues

FRANZ GOLDMANN, M.D.
Clinton, Connecticut

THE RAPID INCREASE in the costs of medical care, in the wide sense of the term, has aroused much concern lately. It is certain to attract serious attention in the near future, as all signs point to a continuation, if not acceleration, of recent trends.

Quite justifiably, efforts to deal with the problem are being concentrated on the widest possible employment of methods designed to achieve efficiency and economy in the various fields of health activities. Such an approach, long overdue, is indispensable. But there is more involved than development of mechanisms that would make the old wheels turn more smoothly. At the core of the problem of mounting costs of medical care are fundamental issues of health policy, some new and some of venerable age. These issues must be resolved.

THE GROWTH OF EXPENDITURES

The total national expenditures for health activities exceeded $35 billion in 1964 and can be expected to cross the $40 billion mark before long. It is of more than academic interest to compare the present situation with that prevailing in 1929, the first year for which comprehensive data were gathered.

In the period from 1929 to 1964, the total national expenditures for all types of health activities have increased almost tenfold, rising from $3,621.5 million to approximately $35,400.6 million. If the analysis is confined to expenditures for personal health services, the same trend becomes apparent, a rise from about $3,304.8 million to approximately $30,566.5 million.[1] Even more striking is the fact that the total national expenditures for all types of health activities have come to represent a larger proportion of the gross national product, probably between 5.6 and 5.9% in 1964 compared with 3.6% in 1929.

In the last few decades, profound changes have occurred in the proportional distribution of the total national expenditures for health activities and in the sources of funds.

In the past, the greater part of all expenditures for personal health services went to physicians. With continued advances in scientific medicine and growth of the hospital as the center of professional services, the share of expenditures received by physicians in private practice declined. By 1929 it represented almost three-tenths of the total expenditures, still constituting the largest portion of the health dollar. By 1962, expenditures for hospital care occupied first place, absorbing one-third of all expenditures for health activities, and expenditures for services of physicians in private practice ranked second, accounting for two-tenths of the total.[2]

As voluntary health insurance spread, benefits paid by insurers increased from an insignificant proportion in 1929 to an amount equal to about three-tenths of all private consumer expenditures for personal health services in 1964. Tax funds, too, have grown markedly. In 1929, they provided the wherewithal for about one-seventh of the total national expenditures for health activities, and by 1964 their share had risen to about one-fourth. Even more rapid was the advance in the proportion of tax funds spent on personal health services—from about one-eleventh to more than one-fifth of the total. Reflecting the wider development of organized payment plans in recent times, direct payments by patients declined from close to 88% in 1929 to approximately 50% of all private expenditures in 1964.

One more highly important change must be mentioned, although comparative data for 1929 are not available. The national expenditures for performance of medical and health-related research have been mounting rapidly since the end of the 1940s. They accounted for close to one-twentieth of the total national expenditures for health activities in 1964.

FRANZ GOLDMANN *is associate professor of medical care, emeritus, Harvard School of Public Health.*

A great variety of factors combined to cause, or contribute to, the rapid growth of expenditures for health activities during the last few decades. The population has increased substantially. The standard of living, and with it the ability to pay for personal health services, has improved markedly, as shown by the increase in per capita disposable income (income after personal taxes). Better education in general and spread of health education in particular have brought about greater willingness to spend money on health services. Rapid development of organized payment plans under the auspices of voluntary and public agencies has made existing demand for available personal health services effective and spurred new demand for health services formerly regarded as luxuries. Tremendous scientific and technologic advances have made medical care in the wide sense of the term more complex, more effective, and more costly. The price of health service, especially that of hospital care, has gone up sharply, in recent years much more than general prices and per capita disposable income. The decrease in the purchasing power of the dollar has contributed to the increase in expenditures for health activities but, after adjustment for this development, it becomes clear that the "real" expenditures have risen greatly.

MORE SPENDING

Are the American people spending too much or too little on health? If considerations other than economic are omitted for the purpose of this discussion, the goal of modern health policy may be defined as the systematic increase of assets—the human capital—through prudent investment and wise spending and, with it, the continued decrease in liabilities—the indirect costs of illness. What proportion of the gross national product should be allowed for health purposes? For instance, would 6% be "reasonable" or "reckless?"

Huge as the actual expenditures for all health activities are, they are low in comparison with the indirect costs of illness—the staggering losses in production, earnings, aggregate working years, and taxes and the enormous sums spent on income maintenance of temporarily and permanently disabled people.

Of the many pertinent calculations, those recently made by the President's Commission on Heart Disease, Cancer, and Stroke illustrate the situation very well.[3] Heart disease and cancer alone were responsible for losses in output by members of the labor force that equaled the total national expenditures for all health activities in 1962, and the direct costs of these diseases, together with the losses in output, amounted to about 5½% of the gross national product. These data state only part of the story. The two "loss leaders" caused additional indirect costs that are known to be large but impossible to calculate.

Obviously, a strong case can be made for heavy spending on all those activities which hold promise of easing the appalling burden of indirect costs of illness, even if this requires an increased commitment of the gross national product. At the same time, every effort must be made to effect savings in the organization, utilization, and administration of health services.

As abundant evidence shows, there is much waste, both sinful and innocent. One group of needless expenditures can be reduced to a minimum through introduction and general employment of better methods. Examples of such waste are the construction of new and expansion of existing hospitals and the duplication of highly specialized, costly hospital equipment without regard to the overall needs of the area; the utilization of hospital beds without strict medical indication; the neglect of determined active treatment of patients in a number of mental hospitals; the obsolete methods of operating out-patient departments in many communities; and the lack or inadequacy of systematic arrangements for intraprofessional, interprofessional, and interagency cooperation.

A second group of causes of waste can be successfully attacked only by changes in basic policies. Examples are the exclusion of preventive services by most of the voluntary health insurance plans, the prevalence of cash-indemnity insurance with its inflationary effect on medical charges, the restrictions on amount and period of medical care and the absence of rehabilitation programs under Workmen's Compensation laws in half the states, and the hodgepodge of tax-supported programs for control of diseases.

Reduction of a third category of wasteful expenditures rests on the hope that educational efforts will gradually influence human behavior. The complexity of this task becomes immediately apparent by a look at such data as the exceedingly high rate of motor vehicle accidents resulting in serious disability or death, the heavy consumption of alcohol and cigarettes with their known harmful effects, the huge expenditures for drugs accounting for about a fifth of consumer expenditures for personal health services, and the vast sums flowing into the pockets of quacks.

Clearly, the fundamental issue extends beyond that of deciding on the amount of money to be channeled into health activities. It includes the choice of such policies and procedures as are conducive to attainment of efficiency and economy in the organization and operation of health services meeting high standards. It involves decisions on the best methods of influencing people to avoid needless expenditures and to make full and discriminating use of available resources for care in health and in sickness.

HOW MUCH MONEY FOR RESEARCH

Intensive and extensive research in medicine, its underlying sciences, and its social use is, of course, a prerequisite for reducing both direct and indirect costs of illness.

Financial support of pertinent activities has become highly popular in recent years. The taxpayers, through the instrument of government, have demonstrated increasing willingness to furnish the "hard cash" required both for construction of good facilities and for performance of medical and health-related research. The total national expenditures for the latter purpose, excluding the amounts spent by certain commercial companies, have risen from $87 million in 1947 to approximately $1,675 million in 1964. Tax funds, originally defraying less than three-tenths of the total, have come to supply more than two-thirds. Federal funds now contribute all but a tiny proportion of the allocations from tax revenues. Thus, promotion of research has become one of the components of the national health policy. The device of federal grants for research has been used more and more, and nonprofit institutions have become the leading beneficiaries, with medical schools receiving a substantial part of the total.

The experience with federal grants has shown that the principles of tax-support and freedom of research can be reconciled, although administrative difficulties are caused by the multiplicity of individual grants. Thus, the major issue debated in earlier years has been settled. But new issues have come to the fore as result of the rapid growth of research funds.

How much money should be spent on medical and health-related research? In 1964, the funds allocated for this purpose represented about 4.7% of the total national expenditures for health activities. An industrial company would hardly question the wisdom of allowing an amount equal to about 5% of annual dollar sales for financial support of research and development in the expectation that the investment would result at least in improved productivity and larger profits, if not in introduction of a new "sensational" product. Health policy is not, and should not be, guided solely by economic considerations. If, for the matter of discussion, merely the economic losses caused by illness and, especially, by diseases of unknown origin, are taken into account, the wisdom of channeling more funds into medical research becomes manifest. It would be both prudent and economical in the long run to consider at least an amount equal to 5% of the total national expenditures for health activities as a reasonable investment in medical and health-related research in the near future.

The second issue raised by the increase in research funds is that of obtaining and holding competent personnel. At present, the demand seems to exceed the supply, and competition for talent is fierce. Intellectual curiosity, originating power, critical judgment, patience, perseverance, willingness to make personal and financial sacrifices, and ability to endure the suffering frequently ensuing from research work—these are qualities money cannot buy. But adequate grants for training in research methodology and for performance of research can go far toward attracting and holding men and women with the professional and personal qualifications and the spirit of adventure so necessary for research.

The largess in providing funds for research workers has brought into sharp relief a problem of long standing: Can the demands of good teaching be reconciled with those of extensive research work? Preoccupation with research leaves little time for classroom teaching, thereby impairing the quality of instruction. There is great danger in the policy of allowing generous remuneration for full-time research, but not for full-time teaching, and of giving more credit to publications than to performance in teaching. The cold fact is that the rule "publish or perish" has been amended by addition of the order "research or resign." Unless determined steps are taken to reward good teaching on a full-time basis, a dearth of devoted and effective teachers may develop before long.

Investment in fundamental research is, of course, a speculation on a "breakthrough." It has little appeal to those who want to see quick results. But long-term fundamental research, including clinical investigations and biomedical studies, must not be sacrificed for short-term and fragmentary applied research. This necessity seems to be recognized, judging from the type of projects now in progress, but it cannot be stressed too often. It is also important to foster continued and deep research in such questions as the socioeconomic aspects of illness, the behavior of people in health and in sickness, the measurement of "productivity" of various types of health services, the social organization of medical care, and the evaluation of the effect of various types of medical care programs now in existence.

DEFENSIVE VERSUS OFFENSIVE STRATEGY

"Health pays" and "See your doctor early before he has to see you" are some of the slogans widely circulated in an effort to encourage people to take advantage of the many opportunities for prevention of disease and for early diagnosis of unsuspected illness. Yet, service for health maintenance and, in some respects, also diagnostic service have become a casualty of a policy fostering large-scale development of "sickness insurance."

Those modeling so-called health insurance after the pattern of fire or automobile insurance maintain that its aim is protection of people against certain unforeseeable risks which occur relatively infrequently and irregularly and create economic hardship. Services for health maintenance, such as routine physical checkups, are ruled out on various grounds. They are supposed to be foreseeable and, therefore, budgetable by the individual without the device of insurance. They are assumed to be used regularly by every insured person and consequently would be a "total loss" to the insurance carrier, they are ruled out because of the high costs and their effect on the premium rate, or they are disregarded because "no insurance scheme can cover everything." This school of thought, predominant at present, actually promotes sickness insurance, not health insurance. It repeats the ideas guiding the development of compulsory sickness insurance in many foreign countries at the end of the nineteenth century and in the early part of the twentieth century and ignores the changes made by a number of these countries since that time.

The arguments advanced against coverage of services for health maintenance are challenged by a minority group, led by the advocates of group-practice prepayment plans. They maintain that it is logical, wise, and economical to prevent diseases causing "losses" and to reduce, if not prevent, expenses for prolonged treatment. The store of knowledge is so vast now that there are ample opportunities to construct health as well as reconstruct it. What is needed is adaptation of the device of insurance to the particular requirements of personal health service rather than continued use of insurance merely as an aid to sick people in paying certain bills. This involves removal of barriers to health maintenance services, discovery of unsuspected illness, early diagnosis, and prompt treatment, including rehabilitation. The problem can be solved. It is one of price and organization.

What has been said about the concept of the aim of insurance also applies to the idea underlying the development of medical care as part of tax-supported programs for the control of certain diseases of socioeconomic importance. Maintenance, if not enhancement, of health is made difficult by the policy of establishing more and more programs of medical care that place the emphasis on particular diseases of the person rather than on the person in need of health service.

The time has come to tear down the Maginot Line behind which most medical-care programs, under the auspices of public and private agencies, are patiently waiting for the attack in the form of a more serious illness and to go over to the offensive.

QUANTITY VERSUS QUALITY

The barrage of claims and counterclaims on the merits of voluntary insurance, compulsory insurance, and taxation for health purposes beclouds the real issue involved. All three are methods of organizing payment for personal health services. Their value depends on the degree of protection afforded and the quality of the services rendered to the people.

Voluntary insurance, compulsory insurance, and taxation, although differing in many respects, are alike in their aim. All are methods designed to tap, assemble, combine, and make effective the financial resources of large numbers of people with widely varying incomes. All result in quantitative gains through distribution of more service to more people. All may lead to mass distribution of inadequate service unless they are combined with methods promoting high quality. Without arrangements for supervision, any method of payment may involve misuse by people who want to get the most out of the program or by physicians who tend toward "monethics," that strange offspring of the union of money and ethics.

The issue, then, is attainment of "the best," not "the most," for the medical dollar spent. The biggest task ahead is to combine the better with the more, and this requires organization of service as well as payment, together with creation of an administrative machinery assuring high standards, efficiency, and economy.

Blue Cross, Blue Shield, and the commercial companies selling health insurance policies are acting as instruments for convenient payment of specified medical bills. Being solely concerned with economic aspects of personal health service, all these organizations expect, or hope, that high standards of service will be assured by some other agency, such as the hospital, and by the bodies representing the professions involved. Essentially, the same situation prevails in the field of public medical care, particularly the programs for recipients of public assistance in its various forms.

The services rendered to hospitalized patients can be assumed to meet generally accepted standards if the hospital is accredited and the professional activities in it are subject to supervision and self-evaluation. However, many people are admitted to nonaccredited hospitals, strict supervision and self-evaluation of professional services are not universal, and even in accredited hospitals the quality of services is not always as high as it should be.

As most of the personal health services—about 80%—are rendered to people who are not hospitalized, maintenance of high standards outside the hospital is of utmost importance. The need for determined action toward this end is widely recognized, but very little has been done up to now. The outstanding exceptions to the rule are the group-practice prepayment plans with their policy of interlocking organized service, organized payment, and administrative procedures for attainment of high standards, efficiency, and economy of health care.

With the passage of the Social Security Amendments of 1965, the issue of quantity versus quality of service has assumed increased importance. Whether it will be brought nearer to a satisfactory solution under the impact of the new legislation remains to be seen.

CASH BENEFITS VERSUS SERVICE BENEFITS

At present, cash-indemnity insurance is carried by the majority, possibly more than two-thirds, of the people covered by voluntary health insurance as distinguished from disability insurance. This is so primarily because commercial companies indemnifying policyholders for medical bills occupy first place in enrollment for hospitalization and surgical-expense benefits and dominate the field of major medical expense insurance. Furthermore, a substantial proportion of the people covered by Blue Shield plans are eligible for cash benefits only, because many of these plans limit full service benefits to members below a certain income level.

Cash-indemnity insurance is essentially a device for trading dollars—the payment of specified, fixed sums of money at the time of a specified contingency in return for the premium paid. It affords a high degree of protection to the insurance carrier but not necessarily to the insured. The spread between cash benefits allowed and charges made by professional persons or hospitals may become exceedingly wide, and the insured may be left with substantial bills at the very time he is least able to pay them. Actually, the out-of-pocket expenses to be met by the insured, especially those requiring hospitalization and surgery, often exceed the amount of the annual insurance premium and are frequently very high, posing a serious threat to the living standard of the insured.

Cash-indemnity insurance may have an inflationary effect on the total costs of medical care, because physicians or members of other health professions may raise their charges to the patients on the grounds that reimbursement will take care of part of the bill.

Full-service benefits protect the insured against unpredictable, annoying, and possibly burdensome additional expenses for services covered by the plan. The costs of such guaranteed service are higher than those of the benefits offered by the typical cash-indemnity plan. They may create a problem to the insurance organization if the rates to be paid to those rendering the services go up. Yet, the social purpose of voluntary health insurance can be achieved only if full-service benefits are made available on the widest possible scale. This ideal is far from realized. At present, only the minority of the insured people are eligible for a few types of full-service benefits. Unfortunately, the new "Medicare" program fails to provide for full-service benefits, and this deficiency is certain to become the subject of much debate in the near future.

PROFIT MOTIVE VERSUS NONPROFIT MOTIVE

What ever became of the nonprofit motive in establishing and operating facilities for long-term care, such as skilled nursing homes, and in developing voluntary health insurance?

For many years attention has been called to the urgent need for large-scale construction of high-grade facilities for long-term care of those patients with prolonged illness or chronic disability who do not need hospitalization and cannot receive proper care in their own home.

The call to action has found ready response from individuals and corporations looking for a business with prospects of a nice profit. Proprietary nursing homes have been mushrooming in many parts of the country. They are the principal resource for long-term care in a special facility. In 1964, proprietary homes provided more than seven out of ten beds for skilled nursing service. Their standards ranged from unacceptable to outstanding, but substandard homes contained a substantial proportion of all beds.

The recent appearance of financially strong entrepreneurs may well serve to improve the standards of care for those patients who can afford the high rates charged and will force some of the substandard homes out of the market. The introduction of accreditation will have beneficial effect in the long run. Meanwhile, the agencies making third-party payments to skilled nursing homes are confronted with two alternatives: setting minimum standards for homes to be used so that large numbers of patients can be admitted or setting optimum standards, thereby sharply limiting the usable bed capacity for long-term care in skilled nursing homes.

The huge proportion of beds in proprietary nursing homes is in sharp contrast to the tiny proportion of hospital beds in proprietary institutions. For centuries, social philosophy has placed the emphasis on development of nonprofit hospitals. What are the reasons for the tendency of communities to abdicate responsibility for establishing nonprofit nursing homes or similar facilities? The issue is not whether proprietary nursing homes should exist. There is a place for them. The fundamental question to be answered is this: Should the profit motive or the nonprofit motive be the principal guide in providing for the necessary number of beds in skilled nursing homes meeting high standards?

Essentially the same issue has come to the fore in the field of voluntary health insurance. In the early stage of development, the nonprofit concept received primary attention and, accordingly, nonprofit plans dominated the scene. Since the 1950s the insurance industry has been gaining ground steadily. At present, commercial insurance companies are not only leading in enrollment for the two most common types of insurance coverage but also are responsible for payment of nearly one-half of all benefits, excluding "loss-of-income" benefits.

Obviously, the voluntary way has become more and more the commercial way. Quite apart from other issues, such as the previously discussed issue of cash indemnity versus service benefits, the rise of commercial insurance to predominance in certain types of coverage makes it inevitable to take a stand on the fundamental question of social philosophy: Should the profit motive or the nonprofit motive be the principal guide in establishing and operating voluntary health insurance?

A NOBLE IDEAL

It does not require a crystal ball to predict that the years to come will see intensified efforts to adapt medicine and the related sciences to social needs and uses. Countless are the pronouncements that adequate medical care should be readily available to all at a price all can afford. Although the objective to be achieved is generally accepted as sound, because it is considered essential to the well-being of both the individual and society, the methods best suited to the attainment of the desired end have been, and will continue to be, passionately debated.

Discussions of methods of organization may easily end on the "narrow road to nowhere," buried under an avalanche of bathos, unless they are preceded by agreement on the meaning of the term "adequate medical care" in the light of modern concepts.

Adequate medical care, as taught by the leaders of the health professions, has 6 clearly definable attributes: [1] It is essentially constructive, aiming not only at restoration of health or, at least, of functional capacity but also at promotion of physical and mental fitness of the healthy, insofar as this is possible with the knowledge at our disposal. [2] It is preventive in the wide sense of the term, avoiding the occurrence of many diseases through protective measures; preventing serious stages, complications, and prolonged illness through early diagnosis and prompt and thorough treatment; and reducing the frequency and severity of disability with its attendant effect on the socioeconomic conditions and behavior of the individual, on family life, and on the well-being of the community and the health of the national economy. [3] Adequate medical care implies continuity of service to the individual in health as well as in sickness, and in all stages of illness, rather than during severe episodes only. [4] It is person-centered rather than organ-centered, paying due attention to the interdependence of mind and body, to the interrelationship of health and environment, both physical and socioeconomic, and to the behavior of the individual in health and under stress. [5] The amount and period of specific services and of all services taken together are sufficient to meet the requirements of the individual. [6] Finally, Seneca's saying, "It is quality rather than quantity that matters," is the guiding principle in rendering personal health service, and the maintenance of high qualitative standards is the mark of perfection.

If these six elements combined make up the

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Evolution in Medical Institutions and Agencies: Emergent Patterns of Cooperation

EDWARD W. DEMPSEY

Washington, D.C.

THE YEAR JUST PASSED has seen enactment of much important health legislation. A White House Conference on Health has taken place in which many challenging new ideas were stated. If the pace of scientific history is an accurate indicator, the challenges ahead will be coming at us harder and faster than ever in the years to come. In scientific and social terms, the year 1990 will be farther removed from 1965 than 1965 is from 1890. The pace of the change ahead of us is obvious.

Despite its recent reputation—soundly or unsoundly based—for rigidity, medicine has bent to the winds of social change since its earliest beginnings. It has been an adaptable art, and it is now an adaptable science. The patterns of practice which Hippocrates taught on the Island of Cos were practicable when the society to be served by medicine was essentially pastoral. The lame, the halt, and the blind could and did seek out the physician whose clinic was under the plane tree; the healer could be called to attend those suffering from accidents; and the ministrations required by the dangerously ill were better provided by priests than by physicians.

Well before the Christian era conditions changed, and, with them, medical practice began its long process of adaptation. The social development of the city-state in Greece and its evolution into the metropolis brought with it the undesirable products of urbanization and crowding—crime and pestilence, mental illness, and epidemics. As they developed, these problems forced society to improvise solutions—jails, asylums, and pesthouses. Both doctors and the body politic had to respond to these new challenges.

Thus, the interplay between government, citizenry at large, and practitioners of medicine—topics as newsworthy as this morning's paper—began millennia ago. What has recently been called the "split mind of medicine"—a kind of philosophical dualism—has been evident for many centuries. Medicare is not too far removed from the steps of the Forum.

The threads of current problems can be traced throughout the Middle Ages, across the centuries to our own time. The medieval and postmedieval study of medicine as it evolved in the semimonastic universities was carefully insulated from the plague victims in the streets. Without straining the ear too much, one can detect a resonance with the contemporary tumult over the gap between the medical excellence existent in university centers and the health care received by people remote from the citadels, the gap between what is known and what is done.

But all knowledge does not derive from theory. It is neither the exclusive property of the thinkers nor the doers. What is done influences what is known. Paré's laboratory was the battlefield; his discoveries came from the hard school of practice. Pasteur responded to the needs of the vintners, the shepherds, and the rabid sick. And to trace the thread across time to the present, modern cardiovascular surgery has taken much of its impetus from the human needs seen in the clinic.

Today, three great institutions, all rooted deeply in a common soil, seek to satisfy man's hunger for a long and productive life. These three—private medicine, the university, and government in its many forms—interact with each other and with the people they serve. The interaction is frequently marked by controversy, by suspicion, and even by open conflict. What is of significance is that despite or because of these frictions, each era has achieved a synthesis which has resulted in a net advance for the human condition.

Today, a new synthesis is being sought, and with an especial urgency, because our present potential for improving the condition of man

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EDWARD W. DEMPSEY *is with the U.S. Department of Health, Education, and Welfare, Washington, D.C.*

DR. DEMPSEY'S *present address is Department of Anatomy, Columbia University, College of Physicians and Surgeons, New York City.*

is incomparably greater than at any previous moment in history. It is precisely this potential which makes failure so bitter and victory so sweet. In spite of this great potential, the goal of providing patient care of high quality often falls short.

For the past year, in Washington, a major evolutionary change in medical partnership has been taking place. The role of the federal government has been sharply altered and, as with most structural upheavals, the initial thrust will undoubtedly be followed by a succession of shock waves throughout the partnership.

Essentially, what has happened is that the federal government, long recognized as a partner in research and, more recently, welcomed as a partner in the construction of medical facilities, is now entering into full partnership for the preparation of health personnel and the delivery of health service. Protecting and advancing the health of the American people has been acknowledged as a national enterprise. The education of those on whom our national health depends has, therefore, become a concern of the nation as a whole. The availability of needed health care—both economically and practically—has been accepted as an appropriate area for governmental support and stimulation. These are evolutionary, rather than revolutionary, developments, and often their logic and even their inevitability can be defended.

The emergent patterns of cooperation now in the process of evolving among medical institutions and agencies are obvious. Dr. Philip Bonnet, in his presidential address to the American Hospital Association in September, called attention to the new synthesis from the vitally important point of view of the hospital resource:

"A new partnership is being forged between the health and hospital service system and the government . . . . As in all partnerships, care and restraint must be exercised by each partner so as not to usurp or obscure the essential conditions and functions for effectiveness of the other partner."

Dr. Willard Rappleye, in a paper titled "Partnership of Government and Voluntary Agencies in Strengthening the Organization of Health Services," states:

"If the challenges of the future are to be met, mere expansion of existing facilities, personnel and programs is not enough. The future calls for fresh approaches, new configurations that would alter—in fact they are already altering—the present patterns and responsibilities of hospitals and a variety of health agencies in the community . . . The challenges require imaginative, unselfish leadership in governmental departments, medical schools, hospitals, organized labor, industry, individual practitioners, and the lay community to insure satisfactory health services in the future."

The desire to work out new forms of collaboration has been manifest, and particularly welcome, in recent statements of the leadership of the American Medical Association. It has been enunciated by university presidents and deans, and by governmental officials at every level. Everyone uses the same adjectives—imaginative, unselfish, creative. Everyone includes the same participants—private medicine, the university, the hospital, the government. But what shall be the shape and substance of the new synthesis? Are the patterns really emergent, or has the chick not yet hatched?

First, I believe that there will be not one pattern, but many, each responsive to the special needs and partaking of the special resources of the region it serves. The great strength of a decentralized, pluralistic health structure lies in its creative diversity. To stifle this would be a disaster. The federal partner in these undertakings is accepting its new charter without losing sight of these values. The view from the national window in Washington is excellent for identifying broad trends and major problems. The federal resource is, in the complexity of modern existence, indispensable for fostering and supporting imaginative ideas generated locally. But the specific ingredients to meet a local need cannot be identified from on high, nor can the proper proportions for the mix be determined at long range.

This is the role for which the great medical schools of our nation are particularly well suited. Each is a part of the fabric of its city and region. Most are already strongholds of medical research and, in the teaching hospitals, of excellence in medical practice. It would seem that the medical school is a logical catalyst to bring about the fusion of medical teaching, research, and service for the benefit of a community, a region, or the nation.

The emergent patterns of today are woven from threads representing past achievements. These trends are numerous and are becoming broader and confluent. Dr. Lowell Coggeshall, in a report to the Association of American Medical Colleges entitled "Planning for Medical Progress Through Education," has made a notable compilation of these trends as follows:

Scientific advance. This is constantly accelerating and has made possible medical care more effective than could have been dreamed of a few decades ago. The use of antibiotics to control and to prevent communicable diseases, the development of occupational and environmental medicine, the emergence of new kinds of care such as cardiovascular surgery, and the appearance of a host of procedures permitting greatly enhanced diagnostic precision—all these and many others illustrate how profoundly science is affecting medicine.

Health expectations. These are constantly and rapidly increasing. Scientific advances, now well publicized, have made the public aware that disease does not have to be endured, that hazards to health can be eliminated, and that bountiful health is at least one requisite of a burgeoning economy. Moreover, the increasing size and urbanization of the population have increased the demand for health services and have made them more readily accessible. As these expectations have risen, an attitude of entitlement is becoming prevalent. Individuals believe themselves entitled to health protection, just as they expect police and fire protection.

Specialization. This is a trend in medicine which has been apparent for decades. The rapidly increasing body of medical knowledge now available causes doctors—including teachers and scientists—to limit their activities to fields in which they have had special training. This trend has grown rapidly since World War II. Today, more than 8 out of 10 new physicians elect to become specialists, and of those who originally enter general practice, an increasing number return to teaching institutions in order to qualify for specialty certification. The trend is responsive both to the physician's desire for excellence—to practice the best medicine he can— and to the patient's desire to have the best care that is available.

Institutionalization. Health care appears in many forms and is a result of many forces. Specialists of different kinds can combine their efforts in group practices, clinics, hospitals, or other institutions and thus provide care more comprehensive than that by any of them alone. Ease of transportation, efficient availability of expensive equipment, ready organization of procedures requiring teamwork—all of these are leading irresistibly toward institutional provision of health care.

These and other trends are reshaping medicine today as it has been continuously reshaped in the past. Out of the needs of the public and depending upon current capabilities provided by scientific understanding, medicine constantly becomes more effective.

The medical school and its federal partner are new ingredients in the developing pattern of medical care. To assume its emergent role properly, the medical school must reorient its thinking and remobilize its resources. It must enlarge, it must engage its activities with the larger and more practical problems of its community, and it must undergo a quantum expansion in its involvement with graduate training and patient care.

Dr. Robert H. Ebert of Harvard, while dedicating a new unit of the Children's Hospital Medical Center in Boston, recently asked: "It is now assumed that the student's education will continue after graduation. Who assumes the important responsibility for this continuing education which now involves as many years or more as have been spent in medical school, and who should have it?" The rhetorical question answers itself—the medical school must continue its educational programs.

The federal partner now stands ready to increase its assistance to medical schools. The Health Professions Educational Assistance Amendments (PL 89-290) authorize scholarships for medical students and provide direct assistance to medical schools through basic and special improvement grants. Construction funds for teaching facilities will continue to be available and in much larger amounts. Medical libraries will receive financial support through provisions in PL 89-291. Among other things, this act will stimulate markedly the ways in which information stored in libraries can be rapidly retrieved and selectively made available to the users.

The new legislation authorizing federal support of regional medical programs to deal with heart disease, cancer, stroke, and related diseases is also predicated on the conviction that the best care is provided in environments where teaching research and service all are fostered. This was, of course, the principal innovative feature of the recommendations made a year ago by the President's Commission on Heart Disease, Cancer, and Stroke. It is designed to bring within reach of physicians and patients, region by region and community by community, the very best in diagnosis and treatment. It calls, not for superimposing a new system of medical care upon a region, but for strengthening and coordinating existing resources. Each regional program is to be based on a major medical center. The role of leadership in reorienting the medical resources of each region will, in most cases, be assumed by the people in academic medicine.

The medical schools of the nation are on the threshold of their greatest challenge. There are

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Implications of Evolution in Medical Care for the Physician of Tomorrow

RAYMOND D. PRUITT, M.D.
Houston, Texas

> *"We need to be very careful what we want for we shall surely get it."**

This inscription, superficially so bright with promise, is, when viewed in a somber light, one of man's bitterest comments on the enormity of his own bent to folly. We fail not because we are overwhelmed by the predators of time and circumstance, but because we mistake evil for good and change for amelioration.† Yet even when conditioned by such warning to the imminence of folly, man, to his credit, has not been long deterred from efforts to shape a future in accordance with his image of the ideal.

I am one with those who believe that a primary concern of this generation of physicians should be a fostering for the benefit of our successors of a professional climate which will attract the finest of human mind and character. With an acknowledged bent to the captious, I have found cause for concern in a title so obviously benign and uncontrived as "Implications of Evolution in Medical Care for the Physician of Tomorrow." Could it just be possible that the future of a noble profession will be rightly fashioned by processes as elemental and impersonal as natural selection? Must Tomorrow's Medicine attract its physicians to a professional environment created to achieve what society in all its understandable concern for the wishes of the majority has designed to meet that majority's needs? I would think it should be and hope it might be otherwise.

Yet we of this generation of physicians have conceived so great an attachment to what was good and right in the past that our near exclusive goal has been preservation of established values. And thereby we have foregone a broad and aggressive leadership in design of medical care for the Society of Tomorrow. We have, as Lindsay Beaton said, waged a determined fight against being hauled by our hair into the twentieth century.[4]

Fortunately the pace of change has been slow and on those matters where the physician's counsel carries distinctive merit because it derives from experience and insights peculiar to his professional role, the major designing remains to be done. Alongside the implications for the physician in an evolving program of medical care we may rightly display the physician design of a professional image worthy of emulation by the bright, the ambitious, the wise and compassionate youngsters we would recruit to our profession. If we fail of attracting these, we shall experience personal sorrow and humiliation, but society's losses by comparison will render inconsequential our own.

AN ACCEPTANCE OF THE INEVITABLE

If valid definition of the inevitable can be achieved, then debating acceptability of a supposed alternative must surely represent an exercise in futility. So confronted, we may rightly accept Carlyle's reputed counsel when told of the old lady who had announced in the elation of newly revealed insight that she accepted the universe. Carlyle replied, "She'd better." As predictions of the inevitable, I shall record 6 propositions pertaining to Tomorrow's Medicine and

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RAYMOND D. PRUITT *is with the Baylor University College of Medicine, Houston.*

*Authorship of this observation is variously ascribed. Dr. Wilder Penfield[1] stated that Dr. Alan Gregg once remarked, "Goethe held that it is important to know as much as possible about what you want most of all because sooner or later you are so likely to obtain it." J. Frank Dobie[2] observed, "When I was a very young man I found a sentence in Emerson that puzzled me then and awes me now, 'Young man, be careful what you want, for you will surely get it.' "

†Paraphrase of Emerson: . . . "but this change is not amelioration."[3]

the physician's role in it. Because I hold them self-evident truths does not preclude possibility that certain reasonable men may think otherwise. But this is an essay and not a debate; and if, in my singleness of mind, I discern no proper alternatives, I could hardly be expected to record telling rebuttal to my own convictions. Here they are.

1. American society wants for all its members the best of medical care. In full recognition that the costs will be high, its members have concluded resources essential to pay those costs are at hand. That society may, in its blindness, provide inadequate rewards in money and status to members of other professions—teaching and the ministry, to mention notable examples. But for hospitals, for physicians, for medical research and development, payment will be made, even prodigal payment, if there is chance thereby to improve the quality of medical care. Individually and locally, exception to this identified course can be found, but the mind of our society is easily read and is evidently committed.

2. Even the existing scope of medical knowledge and skill renders obsolete the concept of the complete physician, competent to do all things for all his patients. An isolated physician is a physician inadequate to the provision of the best of medical care to a community of patients.

3. A community of patients necessarily isolated from the resources of a diversified, potentially cooperative community of physicians no longer exists. Highways, skyways, and the luxury liners which ply them, within the duration of this world's sanity, are with us to stay.

4. The development of highly structured, closely integrated associations of physicians is an established means of providing the highest quality of medical care to a community of patients. If we are seeking a therapeutic democracy in the sense that any patient who brings his problem to the physician is as likely as any other patient, however exalted or humble, to receive the best of medical care, then the closely integrated clinic with a strong central administration is the organizational means to that end.

5. Within this highly structured association of physicians, the role of the several medical and surgical specialists is clearly defined. Their skills and their achievements are so evident and indispensable an asset to society that to undertake without them dispensing the finest of medical care would be ridiculous. Within the day by day assumption of their responsibilities is sufficient challenge to intellect and craftsmanship to keep these physicians alert, stimulated, and self-respecting. Effective discharge of those duties will result in accomplishments satisfying to the patient and impressive to his family. For these specialists in the field of medical practice, the future holds evident assurance of a productive, contributing role recognized as such both by practitioner and patient. Predictably also these specialties will continue to attract and hold their reasonable share of the gifted and ambitious students of medicine, so the pattern of their survival as flourishing professional guilds is complete.

6. Within the highly structured association of physicians, some one physician must direct the individual patient's diagnostic studies, appraise his needs for consultation with appropriate medical and surgical specialists, correlate the judgments rendered by these specialists, and develop and supervise those therapeutic programs which are the patient's reward for submitting to all that has gone before. Ideally this same physician will fill this same role for this same patient over long periods of time. He will be at all times the patient's primary and personal physician and counselor.

No one who understands the functional necessities of a highly organized and effectively working clinic would question the inevitability of the personal or primary physician as a key member of its staff. He is more than a key member: he and his kind are determinative members, so critically placed in the total operation that they dictate by their performance the overall size and quality of the program which the clinic can mount.

Nor does the American medical scene in the year 1965 provide an established and widely accepted pattern for recruitment, training, professional responsibilities, goals, and rewards of this category of physicians. So it is here we depart from inevitables in our projection of medicine's future and the physician's role in it; we depart these inevitables to enter the trying and uneasy business of choice among divergent possibilities.

A MATTER OF ALTERNATIVES

In the years since World War II, both British and American medicine necessarily have responded to the challenge of the increasing complexity of medical care. At the admitted risk of oversimplification, let us ignore the evident divergence of course adopted by the 2 countries in financing of medical care, and proceed to another divergence which may prove of greater and more enduring significance. This latter contrast concerns the role in the postwar period of those physicians, on the one hand, who are specialists in the field of internal medicine and, on the other, those who are general practitioners. In England the successful internist is consultant to a hospital service and clinic to which are referred only those patients deemed by the general practitioner to require diagnostic and therapeutic programs of a complexity beyond the limits of his simple office practice. The internist is able to devote the majority of his time and efforts to study of problems of such severity and complexity as to tax his diagnostic acumen and foster his therapeutic skills. In such a setting he is assured a place among the elite of clinical medicine. But this position is his because the bulk of minor medical problems is being handled by the general practitioner. That same general practitioner no longer participates in the care of the hospitalized patient. He has become a second class citizen among his professional brethren. His preservation, numerically speaking, is assured by severe limitation of the number of consultant posts and the relegation to general practice of those who never train for the consultantship and those who train but fail of obtaining an appointment even after years of hopeful waiting.

The past twenty years in American Medicine has seen changes of equal significance even though these have not resulted from governmental edict. The general practitioner has fought hard and resourcefully for preservation of his traditional privileges; within the considerable latitude of our loosely structured programs of medical care, he has continued to practice a diversified kind of medicine both in and out of the hospital. In American Medicine, the threat to the general practitioner is not relegation to second class citizenship within his profession, but rather extinction by the simple but inexorable process of failing to reproduce his own kind. Meanwhile, the numbers, both absolute and relative, of young physicians entering and completing training in fields of the specialties have risen steadily and the field of internal medicine has attracted the largest numbers of all. The certified internist has little trouble commanding a hospital appointment, and by virtue of working long and hard in his office, he screens out a reasonable number of patients whose illness rightfully warrants hospital care. Nonetheless, I would speculate that the duties of the average American internist are severely diluted by time consumed in caring for patients with minor illness when these duties are compared with those of a consultant on the staff of a British hospital. Moreover, as the ranks of the American general practitioner are thinned and those of the internist grow, the internist will move inevitably and increasingly into the role of the personal or primary physician. We in America will have avoided thereby an outright creation of a two-class citizenry among practitioners of medicine, but we will have placed the specialty of internal medicine under threat of decadence by diluting out the time and energies of its practitioners in disposition of problems which may fail to challenge their diagnostic and therapeutic skills.

As an internist I am much concerned with this evident threat to the future of my specialty. I am not so concerned, however, as to seek its resolution by creating a category of second class citizens, physicians who would man the screening stations and select for the internist those patients ill enough to merit the exhibition of his skills. Deliberate creation of such a second class citizenry is a course at odds with every tradition of our profession, a course unlikely to win support either from organized or academic medicine, a course which negates our idealistic claim that every physician shall engage the challenge of excellence even if some inevitably will engage it more effectively than others.

THE WAY OF EXCELLENCE

And so it is with justifiable concern the internist of 1965 acknowledges that from the ranks of this specialty must come the personal and primary physician of Tomorrow's Medicine. Moreover, we who are internists are only heroic fools if we presume to accept this challenging responsibility only to proceed to discharge of our duties in the traditional patterns of a medical practice now outmoded. The primary or personal physician does occupy a key or determinative position in any adequate program of medical care. From this position he should be able to promote policies which will foster developments propitious to the future of himself and his professional colleagues. So important is the goal that some experimental programs in delivery of medical care should be organized with the primary aim of creating an environment in which this kind of physician finds the richest yield of those professional rewards appropriately meaningful to him. For once, let the needs for the services of the personal physician be fitted as precisely as possible into the overall design of his professional career, so reversing the established pattern of fitting his career to institutional or community requirement for service he must render or demand. The stakes, let me repeat, are high. The survival of medicine as a learned profession attracting to its membership proportionate numbers of the best of each new generation depends upon preservation of the image of a personal, humanistically as well as scientifically oriented, physician.

Suppose we drew the uneasy assignment of designing an institution which would come as close as ingenuity and imagination could bring it to being a setting ideal for achieving the professional gratifications of the personal physician. How would we set about such an assignment?

I believe we should begin with that organization in which the best of medicine is likely to be practiced: the highly structured, closely integrated hospital clinic. Within this organization, the personal or primary physician would assume the full range of responsibilities borne by specialists in internal medicine. He would participate actively in educational programs, both undergraduate and graduate, and in clinical research. His clinical responsibilities would include supervision of diagnostic and therapeutic studies not only of outpatients but also of hospitalized patients.

But certain adaptations would be essential to reconciliation of the internist's concept of his legitimate professional responsibilities on the one hand, and, on the other, the character of the responsibilities he would bear if he devoted much of his time to functions currently assumed in office practice by the generalist. I shall propose three adaptations—two of which, I must acknowledge, would be regarded as a threat to the preservation of what the personal physician of the past and present ofttimes has considered his inviolable image: the concept of the physician as entrepreneur and his patients as the stuff from which he builds his private dominion, a dominion peopled by loyal, admiring, contributing subjects. That this traditional concept must be adapted to the evolving demands of excellent medical care seems inherent in the context of inevitables defined earlier in this discussion. Corollary to the proposals which follow is acknowledged obligation to preserve in strength the personal relationship between the physician and his patients.

1. Critical to achieving his own professional goals is the personal physician's readiness to share with other internists certain prerogatives in the care of his patients. A primary act of sharing would entail acceptance of a ward system for hospitalized patients, a system essential to development of a clinical team made up of the personal physician, house officers, students, and representatives of the clinical laboratories. By entering his patients on such a ward service the internist will have contributed to their chances of receiving the highest quality of care. He will have secured for himself the privilege of acting at regular intervals as the attending physician in charge of such a service. During such periods he will profit from interchange inevitable among members of such a clinical team, functioning as it does in a setting of intimate and personal struggle with the problems of individual patients. No refresher course is likely to provide so effective a stimulus as this to the physician's maturation into an informed specialist capable of applying wisely advances in medical care.

2. Some thinking unfettered by the restraining forces of custom should be devoted to the possibility of the personal physician sharing with nonphysician personnel certain of his established functions in the outpatient clinic. If this proposal is carried to the level of specifics, the consequences are likely to be incendiary. But inescapable is the imperative for appraising critically how essential to every task now performed by the internist is his long, intensive, and costly training. Where others could act effectively in his stead, they should be trained to so do. To acceptance of this course, the alternative is engagement by the physician of the hazard of self-destruction in a frantic display of presumed omniscience and omnipotence.

Having encouraged maximal use of paramedical personnel as skilled assistants to the personal physician, I am obliged to comment also on what might be achieved by processes of automation in data collection, analysis, interpretation, and retrieval. Willing as I would be to accept help from any quarter so long as it reduced the hours presently spent by the personal physician in gleaning information from and about his patients, my hunch has it that in this highly personalized undertaking, major and effective help will come from well trained, capable people—not from machines no matter how ingeniously designed.*

3. To many internists the most unrewarding part of outpatient clinic practice is care of the large number of patients with "functional" problems. The physician's aversion to caring for these patients stems only in part from the evidently valid assertion that an unpleasant turn of personality is inherent in the illness of certain of

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*This comment is directed specifically to the problem under discussion, namely, the possible delegation of the multitude of acts currently performed by the physician himself for his office patients. I am suggesting these personal acts by one human being in behalf of another must continue to be a function of human beings. I am not engaging the topic of the use of computer science in storage, analysis, interpretation, and retrieval of clinical data.

them. Of greater consequence is the frustration shared by physician and patient alike in the inadequacy of existing therapeutic methods for management of many expressions of functional illness. I wish the future held greater promise for relief of this mutual frustration by way of improved psychotherapeutic or pharmacologic approaches. I am pessimistic in this regard and if my pessimism is unjustified, then the internist will surely be a delighted citizen of this brave new therapeutic world.

Reconciliation between the internist and the problems of the patient with functional disease may better be sought in administering that internist a benevolent and enlightened conditioning, brainwashing to the cynical, to his obligations and resources in the care of such patients. At some reasonably early and formative phase in his professional training, he should have exposure, both intensive and prolonged, to senior internists with great interest and skill in the management of patients with psychosomatic disease. To the degree the future personal physician identifies with these senior figures, adopts their attitudes, acquires their skills, and nurtures assurance of his competence as counselor to the emotionally disturbed patient, to proportionate degree he will accept and relish his responsibilities with this category of patients who are so major a component of outpatient clinic populations. For many of them, intensive, long-term psychotherapy as conducted by the psychiatrist may be neither a practicable program nor an assuredly rewarding one. The personal physician's responsibility to these patients and their progeny of Tomorrow's Medicine will be both great and singular. He may rightly prepare to accept that responsibility and like it . . . or better still, love them.

TOMORROW'S PHYSICIAN

I have said little about the part which colleges of medicine should play in the development of personal physicians for Tomorrow's Medicine. I believe the abundant prestige and influence of the academic enterprise must be committed to nurture of such physicians. Ascendancy of the full-time concept in clinical departments of medical schools will validate the aspersions of its discerning opponents only if it generates preferentially and excessively a cadre of academically elite who are not fully physicians. Academic medicine's answer to this potential detraction should be the well trained, strongly motivated, personal physician of Tomorrow's Medicine. We of the full-time faculty must ourselves meet the threats of specialization, fragmentation, and detachment. If we are successful in meeting these threats, then by what we are we shall foster a breed of physicians who personify for patient and for society a synthesis of abstract scientific accomplishment with a personal ministry to the sick.

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The Mounting Costs of Medical Care: Fundamental Issues

Franz Goldmann, M.D.

concept of adequate medical care—and no evidence to the contrary has yet been offered—then they must be made integral parts of any and all organized programs of medical care, regardless of auspices. This is the great challenge to be met by American health policy in the future. Some persons may once and for all dismiss the idea as utopian. Many observers of the contemporary scene may be inclined to wait and see. Their reluctance to touch the many vexing problems is increased by the fear that blunders made in the past may be repeated in the future.

To postpone the solution of pressing social problems because of formidable technical difficulties is to doubt man's ability to apply to the social organization of medical care the same ingenuity which has produced so much progress in technology.

The intricate problem of organizing adequate medical care for all at a price all can afford can be tackled successfully if it is approached with the same spirit of venture and the same objectivity which have been so effective in solving problems of etiology, diagnosis, and treatment of disease.

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Health Institutions of the Future

RAY E. BROWN

Durham, North Carolina

It is a pleasure to participate in the seventy-fifth anniversary of the celebration of the founding of the University of Minnesota Medical School because this hospital and medical school are considered as one of the top institutions for medical education, research, and patient care in our country.

The health institution of the future will no longer be confined within brick walls. It will be more of a concept than a thing. It will be described more by what it does than what it is made of. It will still have its brick walls, its personnel, and its assorted hardware, but these will not represent its principal ingredients. Each of these will be increasingly more unique, complicated, and sophisticated, but the sum of them all will not represent the health institution of the future. The principal ingredient will be organization. The health institution of the future will be identified more as a set of arrangements for the use of medical resources than as a site for the use of those resources. It will become diffuse because it will have to become more comprehensive. The personnel, equipment, and organization it represents will have to be utilized for all levels of health care, whether for the homebound, the ambulatory, the extended care, or the hospitalized.

The health institution of the future will be directed more toward the ends than the means. Up until now we have organized our resources around our services; this will now be reversed. In the future, services will be paramount and we will utilize the resources in terms of the services and the purposes that the resources should be fulfilling. It will be characterized by being more consumer oriented than producer oriented. Here, it's a matter of better packaging and better marketing of the services that the health institution will have to offer. Some of the medical profession in its organized aspects will disagree, but there is no argument against the fact that the consumer will become the king and that we're going to have to do things the way the consumer can best take advantage of them.

Institutions will be more externally than internally dominated. That is, decision making will pass more and more outside the institution and to the public. It will be more systematized; there will be less segmentation and fractionation of decision making. There will be more subordination of the parts of the system of our institutions to the total community requirements.

Another factor will be intermittent care rather than episodic care. Patients will remain the responsibility of the health care institution, returning for care at whatever level is deemed appropriate, rather than reentering, leaving, and reentering for each episode of illness.

A greater horizontal spread of medical advances will take place. Up until now we have tried to put into use every medical advance that has occurred, with the thought that there would be competition for the new advances and that the advantage would lie with those with the greater resources. In the future we will not move as rapidly toward the implementation of medical advances as we will toward the spreading of these advances across the population. The implementation of the more expensive advances will have to wait until every person has the benefit of the medical advances already present.

Finally, we are going to have much more exciting and satisfying medical institutions. They are going to satisfy the doctor, the personnel, the public, and especially the administration because of a greater sense of accomplishment, a lesser sense of frustration on the part of everyone concerned, and a sense of really taking a position in the mainstream of social well being.

A look at the medical, social, and economic trends will show some of the following facts. The present-day trends are leading to increasing dependence of modern medical care on expensive hardware and highly trained personnel.

RAY E. BROWN *is director of the graduate program in hospital administration, Duke University, Durham, N.C.*

Modern medical practice is literally impossible unless arrangements are made for resources and for needs of the doctor and the patient.

Increasing specialization of medicine requires a meeting ground for diverse knowledge and skills of doctors. There is a growing inability of the patient to discriminate between doctors, and he becomes dependent upon some institutional arrangement for such discrimination and assignment. This involves the proper doctor to go to and has something to do with the control of quality. We now ask the patient to run a medical maze in obtaining care that doctors themselves frankly admit they don't know how to cope. The effect on quality of working in an organizational climate has been shown. This is a matter of visibility—of having others of equal judgment and equal competence looking over the professional's shoulder. Such medical kibitzing will always be the best way of assuring proper quality and proper quantity allocation between patients.

The increasing mobility of the population means that the notion of an individual having his own doctor is rapidly disappearing. Growth of the hospital emergency rooms across the nation demonstrates this. Only one out of nine patients, by most studies, really needed to go to an emergency room, but they went there for medical service because they were medically disengaged from the system of medical care. They needed a coupling device, a point of entry, in order to get into the system, because the great mobility of the population has separated the individual from the system. This mobility is of two sorts. One is geographical mobility. We are a population on the move. We change employers now five and half times during our experience in the labor force. We actually change the geographical region in which we live three times during our lifetime. There is little likelihood of a person having his own personal physician in the future. The substitute will be organizational arrangements to keep the individual coupled into a system of care. We must work out for our voluntary system the sort of efficient coupling device that the veteran has in the veterans hospital. The Veterans Administration system does one big thing—it couples the individual into a system where all he needs to do is to knock at the door and one door only. It becomes highly important that organizational arrangements are provided whereby the individual, once in the system, remains visible, attached, or engaged to the system.

Social mobility, often overlooked, is perhaps more important. Imagine the change that occurs to a person who goes off welfare and loses the help of the social worker who has helped him with the problem of finding a doctor, directed him to a doctor, and seen to it that he remained latched into the medical system. Imagine the problem of the Negro who has had only one route for medical care. Now this route is being rapidly erased through integration. The great social advances that are being made through integration will, at the same time, leave the Negro with the great problem of how to integrate himself into a very diverse and mysterious system of medical care.

A new factor for the health institution of the future is the increasing interest among physicians for more orderly and reasonable personal and professional lives. This is coming far too late. The doctor has been imposed upon by society. The younger doctor of our generation is beginning to revolt against this, and we can expect that organization will be used more and more by doctors as a mechanism to allow them a more orderly, a more pleasurable, and a more satisfying way of life without in any way damaging, and perhaps enhancing, professional aspects.

The increasing sophistication of the public as regards the capabilities of medicine when provided adequate facilities is resulting in a system of facilities geographically accessible to everyone. The growing public recognition that the quality of medical care is better controlled under institutional arrangements is causing the public to increasingly seek its care through such arrangements. Cultural changes in attitudes toward favoring institutionalization of illness and the right of the well to be free of the drudgeries of caring for the sick are leading to an emphasis on our medical and health care institutions as being institutions for convenience as much as institutions for the scientific practice of medicine.

In addition, present-day high standards of living mean that people can afford more medical services and they are going to demand more. Discretionary income usually goes primarily to personal services, and this discretionary income is growing rapidly. Our century may be marked socially by the elimination of poverty. Furthermore, even the middle class has a rapidly rising income. To the extent that dollars affect the quantity and conditions under which medical care is distributed the consumer is now moving into the driver's seat.

Demographic changes are also going to affect the mode and the utilization of medical care. Large increases in the population above age 65 have already forced special arrangements for that group. The even greater increase in the middle-aged is shifting the pattern of illness to the degenerative diseases and, consequently, increasing the length and intensity of medical treatment. It is in connection with these diseases that we can expect our greatest research effort and our greatest medical advances in the future. Medical advances mean that more and more things can be done for people; therefore, more and more things will be done for people as their aspirations increase and financial accessibility increases.

Efficiency as well as effectiveness in the use of our health care institutions is needed. Both in terms of unit costs and in percent of the gross national product required, health costs more and more each year. It is now using about 5% of the gross national product per year. The unit costs are rising even more rapidly than the percent of the gross national product because the gross national product, even with its dramatic growth, isn't growing as rapidly as the factors that influence institutional costs. There is the wage bill—more people are used for the same unit and better wages are paid to the people. One of the shames of the health field has been the low wages that it has paid to its paramedicals and to its ancillary professionals. There will be higher pay and the use of more and more people, because services are going to become more and more complex.

Earlier mention was made of external orientation rather than internal orientation of the decision making for medical care. There are some very clear-cut, logical, rational, and acceptable reasons for this. The first is the growing public interest and concern over good health. There is a growing public awareness that poverty and poor health are closely related. We have seen many times that the person who has lost his health has been thrown on the labor scrap pile and denied the opportunity to participate in a productive way in our society.

Our generation has been condemned for being materialistic. The reverse seems to be true. If any people ever came closer to the Biblical command that we be our brother's keeper, our generation has moved farther in that direction. We now really believe that we should not enjoy the necessities if our fellowman does not have access to these necessities. There is a growing interest to contribute to the welfare of others in some form. Health care is one way we can contribute because health care does respond in a very dramatic way to dollars, to the financial support that an increasingly affluent society can provide.

We are as a nation committed to everyone having reasonable access to reasonably good medical care. This means that society is going to call upon government, if we do not do it voluntarily, to enforce it. Many of our great denominations and our national nongovernmental agencies are dedicated to that same proposition. We can again expect kibitzing in our policy making and decision making and a demand that we live up to a very proper social commitment.

There is a gap between the wonderful voluntary prepayment programs and certain groups of our population—the aged, which we have just done something about, to the disabled, the unemployed, and the self-employed, such as casual labor and agricultural workers. The great progress that has been made by our health care institutions has been largely due to the sound financing that the voluntary prepayment plans provided. Unfortunately, these plans did not provide for all members of the population because the concept of prepayment has to do with the working force. If one studies its history and the way that it is marketed and administered, it is a device whereby the members of the working forces can do a wonderful job for spreading the burden of illness and avoiding the great unevenness that occurs in illness. But there are pockets that do not fit into the concept. Competition between the commercial insurance industry and Blue Cross plans is driving each to constantly seek those who need coverage the least. This means the gaps are not being closed. There is no alternative except to have government work out measures and plans and programs that will enable those who fall between the gaps to enter into and become a part of our medical care system with the same dignity and rights as they would have in the private plans.

It seems that the AMA missed the point entirely in the great argument about the use of the means test in financing medical and hospital care of the aged. It isn't the poor that we're worried about but those who have some resources and whom we hate to see impoverished because they do not have the same prepayment mechanism working in their favor to protect their resources that the rest of us do. The Medicare program is a way of fitting the voluntary system as closely as possible to a prepayment type of approach, of giving the individual after age 65 that same identification card that he had before age 65, and of giving him the passport to adequate and dignified medical and institutional care. Some won't agree with that, but there will be no voluntary system in this country as long as any large segment of the population is involuntarily left out of the voluntary mechanism.

The increased interdependence of the population means we are rapidly becoming our brother's keeper. Maybe we haven't arrived fully at that millennium. Maybe we aren't fully our neighbor's keeper, but we are our neighbor's hazard. As we become more congested, as the population increases, then our problems become our neighbors' problem, whether our neighbors want those problems or not. We're going to have to look to arrangement and organization, both for the securing of the funds and for the utilization of these as we market, merchandise, and distribute the kind of medical care that is possible today. This great interdependence that we are developing means that the future will be characterized by pooled effort, by joint effort, by acceptance of responsibility on the part of individuals for the welfare of the general public. This is seen, in one instance, by the great effort toward systemization of our facilities by planning councils that have been rapidly established over this country. These planning councils may finally have to have a leverage of public intervention through the prepayment and governmental systems of payment or legislative support.

We can expect more and more public involvement because health business is big business. This in itself is reason for serious scrutiny by the public even if no other issues existed. In our health institutions and professions about one out of every forty members of the working force of the nation is employed. It is obvious from just the sheer economic aspects that government has to take a close look and keep its finger closely on what is happening. It shows tremendous interest in what the steel industry does because of the impact on the economy. The number of people employed in the steel industry is not near that of the total employed in the health industry. Look at the economic impact of the health field as a consumer of the products of the rest of the economy and the impact of the health industry upon its community. Those in the hospital field who are opposing the inclusion of hospital personnel under minimum wage laws are wrong. We have no right to impose upon our community a group of subpaid, submarginally participative people. How can they participate as good citizens and good customers if they are going to be made captive philanthropists, if they're going to be denied the fair share of the productivity of the economy? We have no right to plead poor mouth; we have no right to beg off from legislation. Minimum wage laws may make doubtful economic sense, but if this is social policy, then the health field ought to measure up to this social policy if other employers are going to have to measure up to it.

We can expect ever greater public involvement because our politicians are beginning to realize that good health is good politics, and it is, in the finest sense of the word. The growing aspirations of our people toward good health, the realization that good health can be purchased, and awareness that good health has many consequences both for the individual and society at large are obvious realities. In every way, the promotion and the support of good health are good politics. We have a very sensitive, wide-awake group of politicians, and they aren't going to overlook a bet like this. In all fairness to ourselves, let us sincerely hope that they will not.

ERRATUM. In the article, "The Thymus" by Esther M. Greisheimer, Ph.D., M.D., in the September issue of The Journal-Lancet (86:452-456) under "Origin and Development of the Thymus" on page 453, lines 22 to 29 should read "At 22 mm. the formation of leukocytes is proceeding apace in the thymus, and some are wandering into the surrounding mesoderm. By the time the embryos are 25 mm. long emigration of leukocytes is conspicuous. The production of leukocytes becomes more abundant, and the emigration more prominent until the 70 mm. stage is reached."

Administrative Highlights in the Development of the Medical School

HAROLD S. DIEHL, M.D.
New York

FIRST, I want to tell you all how happy Julia and I are to be back home to join with you in recognizing this 75th Anniversary of an institution with which we have been associated for half a century.

It is truly thrilling to see so many wonderful friends here this evening. Some of your kind greetings, however, remind me of a comment that Jim Farley made at a luncheon recently in New York. In introducing him, the master of ceremonies commented upon his wonderful health and vigor for one of his age. In reply Mr. Farley said that he has observed that there are 3 stages in life: youth, middle-age, and the time when your friends say: "My, how well you look."

My association with the medical school began in the fall of 1914 when I came here from Maryland to enroll as a freshman medical student. This was a long time ago. I will, however, not dwell upon this because I remember Mark Twain's remark that "Methuselah lived over 900 years but so far as we know it is the only thing he ever did."

Instead I will comment briefly on what seems to me the more significant influences and factors in the development of our medical school.

To me it seems that these seventy-five years in the history of the medical school divide themselves into 3 rather distinct eras, each covering approximately a quarter of a century. The first we might call the era of organization; the second, the era of reorganization and foundation building and the third, the era of development and expansion. In each of these eras there were leaders with imagination and the courage to experiment and there were critical and dramatic situations in which the future of the medical school seemed to hang in the balance.

During the period of organization four propriety medical schools in Minneapolis and St. Paul were induced to give up their charters so that the university might develop one strong medical school for the state of Minnesota. These were years of bitter controversy and many frustrations but the aggressive determination and perseverance of Dr. Perry Millard and a few staunch supporters finally achieved what for a long time seemed impossible.

The practicing physicians of the Twin Cities who had constituted the faculties of the merged medical schools provided the instructional staff of the new school. Teaching was done in the hospitals and laboratories affiliated with these schools until buildings were provided on the university campus for the basic science departments.

The significant final development of this first quarter century was the establishment of a campus for the medical school to the south of Washington Avenue. At the time this location seemed remote from the main university. Constructed during this period were the original Elliott Hospital and the initial units of Millard Hall and the Institute of Anatomy—now known as Jackson Hall. Today this may seem like a small beginning but it was vitally important because it assured a close and effective relationship between the medical school and the rest of the university.

The second quarter century, which I have called the era of reorganization and foundation building, began about 1913, shortly after George E. Vincent assumed the presidency of the university. After surveying the university's medical school, President Vincent concluded that, if Minnesota was to have a strong and progressive school, it was essential, first, that there be added to the faculty some able medical scientists and teachers who could devote their full time to education and research, and second, that the faculty be reorganized and reduced in size from what he described as essentially a classified medical

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HAROLD S. DIEHL *is senior vice president for research and medical affairs, American Cancer Society, Inc., New York.*

directory of the physicians of Minneapolis and St. Paul. To accomplish this he appointed to the faculty able young men, such as Bell, Jackson, Scammon, Dean Lyon and others, who were towers of strength in rebuilding the school. He then asked for the resignation of every member of the medical faculty and upon recommendation of a special committee reappointed those who were competent and interested medical teachers. This resulted in some stormy sailing for the medical school. However, with wise leadership and dedicated support from most of the physicians of the community and the state, the school survived this radical operation and with a smaller and abler staff proceeded on its course toward becoming a strong, cohesive, and modern school.

Another major development of this era was the establishment of the Mayo Foundation for Graduate Medical Education and Research under the authority and responsibility of the graduate school and the regents of the university. The proposal for such a foundation was made by Dr. Will and Dr. Charlie Mayo in 1914. After more than a year of consideration and negotiation, including some vigorous opposition by certain physicians of the Twin Cities and the state, including a few on the medical school faculty, this affiliation was approved and authorized by the regents. This, however, did not end the opposition and bills were introduced into the legislature to prevent the regents from consummating this affiliation. Hearings on these bills were conducted jointly by the Senate and the House of Representatives in an evening session in the senate chamber. I was a medical student at the time and, together with a couple of classmates, was wise enough or probably just fortunate enough to attend. The opposition, represented by several able and vigorous spokesmen, presented the reasons why, in their judgment, the university should not become affiliated with any private hospital or clinic. Most of these arguments were presented with great fervor and emotion. In reply, Dr. Will Mayo with great dignity, poise, and sincerity explained that many physicians were coming to the clinic for training in the various medical specialties; that a fund of approximately a million and a half dollars had accumulated from the operation of the clinic and that he and his brother, Dr. Charlie, thought that the best way to use these funds for the benefit of the public from which they had come was to give them to the University of Minnesota for the promotion of graduate medical education and research. I remember thinking, as I listened to Dr. Mayo's quiet but effective presentation, how this resembled what I had visualized as the debates in the Roman Forum by Plato and other distinguished orators of those bygone days. The result of these hearings was that the legislature took no action on these bills. Unfortunately, Dr. Mayo did not have a manuscript and no stenographers were present to record what he said. Dean Ford, of the graduate school, in commenting later upon this referred to it as the tragedy of "The Last Oration." Thus, began a most significant program of graduate medical education and research which has brought distinction and respect to the Mayo Foundation and the University of Minnesota throughout the world. Incidentally, the official designation of the Mayo Foundation was changed last year by regent action to the Mayo Graduate School of Medicine.

The third quarter century I have called the era of development and expansion. This was the period during which it was my privilege to serve as the administrative head of the school. As to what was achieved during this period I might say, as was said of Christopher Wrenn, "Look about you." And by "looking about you," I refer not primarily to the buildings and the facilities which they contain but rather to the distinguished and dedicated men and women working in these buildings and the significant and superb work that they are doing—work that is known and respected not only in Minnesota but also throughout the world. I would urge you also to look beyond even this, to note the quality of medical service rendered by our graduates and the contributions in teaching, scientific research, and public service rendered by the many Minnesota men and women who have left us to join the staffs of medical schools, research institutes, public health departments, or organizations elsewhere.

Earlier in my remarks, I mentioned the names of several of the stalwart pioneers in the development of the medical school. I would like to name and pay tribute to those who were the leaders during my administration but limitations of time make this impossible. I have, therefore, concluded that the only solution is not to mention anyone by name.

However, the progress made was by people—people with dreams and ideas, people with the ability, the patience, the energy, and the dedication to converting these dreams and ideas into realities. I spoke earlier of the drama and the crises of the earlier years of the medical school. I can assure you that there were many dramas, crises, and human interest stories during the more recent years of the school's development.

I wish that I had time to tell you about some of these that occurred in connection with the Variety Club Heart Hospital, the American Legion Research Professorship, the Mayo Professorship of Public Health, the Masonic Memorial Hospital, the Veterans of Foreign Wars Institute for Cancer Research, and the Mayo Memorial. None of these significant developments just happened. Rather each was the result of someone's dreams—skillfully, resourcefully, and patiently nurtured and promoted until it became a reality.

As an example, I would mention the largest of these—the Mayo Memorial. It took about fourteen years from the time that Governor Harold Stassen appointed the first Mayo Memorial Commission until this memorial became a reality. And several times during this period the project seemed impossible of achievement and once it seemed completely dead. At this time a chance meeting and conversation that I had with Dr. Donald Cowling, then President of Carleton College, on Star Island in Cass Lake where we both had summer cottages, led to the reorganization and revitalization of the project, which under Dr. Cowling's resourceful leadership, was eventually carried to a successful conclusion.

I might also cite our experience with the Medical-Biological Library as an example of how things sometimes get done. Shortly after I took over the deanship in 1935, President Coffman asked me what building was most urgently needed. After consultation with the faculty, I reported that our most urgent need was for a medical library building so that the excellent collection of medical books and magazines in the main library could be brought to the medical campus where they would be utilized regularly by students and faculty, not occasionally as was true with this collection housed in the main library building.

Funds for the construction of such a building were included in the next university request to the legislature but that legislature made no appropriations to the university for buildings. Then, toward the end of World War II, it was anticipated that after the war Congress would appropriate funds for the construction of public buildings to spur the civilian economy as had been done after World War I. To be prepared to make an early request for such funds, we had plans and specifications prepared for the construction of a Medical-Biological Library in the then vacant corner between the Medical Sciences Building (now called Owre Hall) and the Institute of Anatomy. The anticipated depression, however, did not develop so these plans were never used.

Next, plans were made to house the library in 3 floors of the tower section of the Mayo Memorial Building. These floors, however, were eliminated when, due to the Korean War, construction costs exceeded available funds.

Our next effort was made in 1954 when bills were introduced into the United States Senate and House of Representatives to provide federal funds on a matching basis for expansion of medical school facilities. At this time we decided that the best location for the Medical-Biological Library would be where it now stands at the corner of Union and Essex Streets.

The estimate as to the cost of such a library building was one million dollars. We therefore presented a request of the legislature for $500,000, expecting to get the additional $500,000 from federal funds. In the legislature, the House Appropriations Committee approved this request but the Senate Finance Committee turned it down. This item then went before a Conference Committee.

When this occurred, I was in Washington for several days and had seen Senator Lister Hill and Senator Edward Thye of the Senate Finance Committee and Dr. Walter Judd and others of the Minnesota delegation in the House of Representatives relative to the bills in Congress for medical school construction. They all told me that they thought that these bills would be passed. Then when I arrived back in Minneapolis late one evening, I received a call from Mr. Amberg stating that the Conference Committee had disapproved our request, substituting instead a building on the agricultural campus sponsored by a senator from a rural community who stated that his doctor had told him that the medical school did not need a library.

I immediately went to the state capitol and found Mr. Amberg, Dr. Kottke, and Dr. Kubicek waiting outside of the room in which the Conference Committee was meeting. Rules forbade the calling of anyone out of the meeting. Fortunately, however, one member happened to come out of the room. As he did so, I told him that I had just come back from Washington and that I had been advised that the bill to provide federal funds for medical school construction would doubtless pass and that if our request for the library was not passed at this time, Minnesota would lose an opportunity to get half a million dollars. I added that I had in my pocket a copy of these bills. This member of the Conference Committee, who fortunately was in favor of our request, asked if he might take the copy of these congressional bills into the committee room. Within a few minutes the committee adjourned after having approved $500,000 toward the library.

Congress, unfortunately, then did not enact the legislation as anticipated. In spite of this, during the next two years we prepared plans and specifications and presented a request to the next session of the legislature for the additional $500,000 required. The legislature acted favorably upon this request, so that by adding funds from several other sources, it was possible to construct our superb medical-biological library, the great value of which is obvious to everyone.

There is more that I would like to tell you but time will not permit. So let me just summarize what I believe were the major factors in the progress made during this third quarter century.

First, we were fortunate in having a sound foundation, with the medical school an integral and functional unit of a strong and developing university, located on the campus, and staffed by a nucleus of able medical scientists and teachers.

Second, the medical school has had the continuing support of the university administration, the regents of the university, and the state legislature.

Third, the medical school won the interest and strong support of the citizens of the state, laymen as well as physicians. It is, I think, unique for a state university medical school to have such support as our school has received from private individuals and organizations. This is invaluable and must be nurtured.

Fourth, we were able to develop constructive and effective affiliations with the Minneapolis Veterans Hospital, the Minneapolis General Hospital, the Ancker Hospital of St. Paul, with state mental hospitals, and with several private hospitals in the Twin Cities.

Fifth, during this period federal funds began to be available for the support of medical research and on a matching basis for the construction of certain research and hospital facilities.

And last, and most important of all, we were able to develop a superb faculty dedicated to the best in medical teaching, in medical research, and in the care of patients entrusted to its care. In conclusion, I want to say just 2 more things:

First, that upon returning for this occasion, almost eight years after my retirement, I feel the greatest satisfaction that an individual can possibly have: that is to see the work to which he has devoted his career being carried forward with vigor, imagination, and wisdom.

Second, I admit that I am just a bit envious of the opportunities which Dean Howard and his colleagues will have over the next quarter century. With research opening new vistas in the medical sciences, with increased facilities and support for medical education and research, and with expanding concepts of medical school responsibilities, you have both tremendous responsibilities and opportunities. Your problems are vastly greater and more complex than those of any previous administration but I am satisfied that with your splendid faculty and administration, the next quarter century will produce achievements that will exceed both our expectations and our fondest hopes. So good luck and Godspeed to you all.

Continued from page 545

Evolution in Medical Institutions and Agencies: Emergent Patterns of Cooperation

Edward W. Dempsey

many doubters. There are those who view academic medicine as an institutional culture built upon and oriented toward research to such an extent that it neither can nor will bridge the gap between research and service. There are those within the academic community who still view the university as a sanctuary for scholars, a matrix for ideas whose application lies outside its proper realm of concern. There are many who will be reluctant to leave the warm and tidy comfort of the laboratory for the cold unruly community.

There is a tremendous job to be done, a vacuum of leadership to be filled. Medical education has demonstrated its capacity for responding to challenge may times in the past. It pulled itself up by its own bootstraps following the Flexner Report. It has been the primary agent in carrying out the greatest advance in research knowledge ever generated. It has trained successive generations of the best physicians in the world. It will rise to this new occasion by guiding the adaptation of health resources to the needs of all the people.

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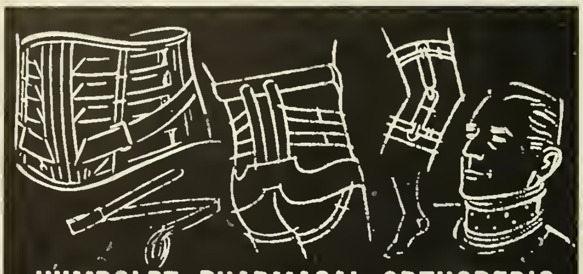

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Book Reviews . . .

Surgery of the Foot

by HENRI L. DUVRIES, B.S., D.S.C., M.D., *2nd ed., 586 pp., ill., C. V. Mosby Co., St. Louis, 1965. $17.50*

This second edition of "Surgery of the Foot" is a worthy successor to the original volume, cognizant of the need for an improved and up-to-date contribution. The author has answered the requests of his many readers and students for more detailed information and precise definitions of the many infirmities that afflict this region of the human anatomy.

Feeling that the foot has been somewhat ignored as an important unit and in great effort to instrument a society comparable to that of the American hand surgeons, he has endeavored to detail the unique disabilities, diseases, and deformities in a knowledgeable manner. His intention to stimulate further investigation in the problem of the human foot is bolstered by the strong conviction that 90% of the forefoot disorders are resultant from ill-fitting shoes.

The presentation has a particular appeal to orthopedic surgeons who are seeing an increased number of patients with painful and deformed feet. The entire subject is presented in an authoritative manner with chapters by contributors who are particularly able to offer practical suggestions for conservative treatment as well as to describe the more refined operative procedures that are a frequent necessity to relieve the symptoms.

In general, the surgical techniques are readily understood. However, accompanying illustrations reinforce the proper image and exacting aspects of the operation that may be more difficult to grasp without visual reference. The format and X-ray reproductions are of splendid caliber. The subject matter is presented with scholarly background and is a welcome addition to the orthopedic library.

The population increase, longevity, and flamboyant tendency for manufacturers to produce shoes with cosmetic appeal rather than comfort all militate for a thorough understanding of the problems of the foot. All those who desire a book that is comprehensive and readily understood will do well to have this reference easily available. It is expedient and highly recommended.

HARVEY O'PHELAN, M.D.
Minneapolis

The Acute Abdomen for the Man on the Spot

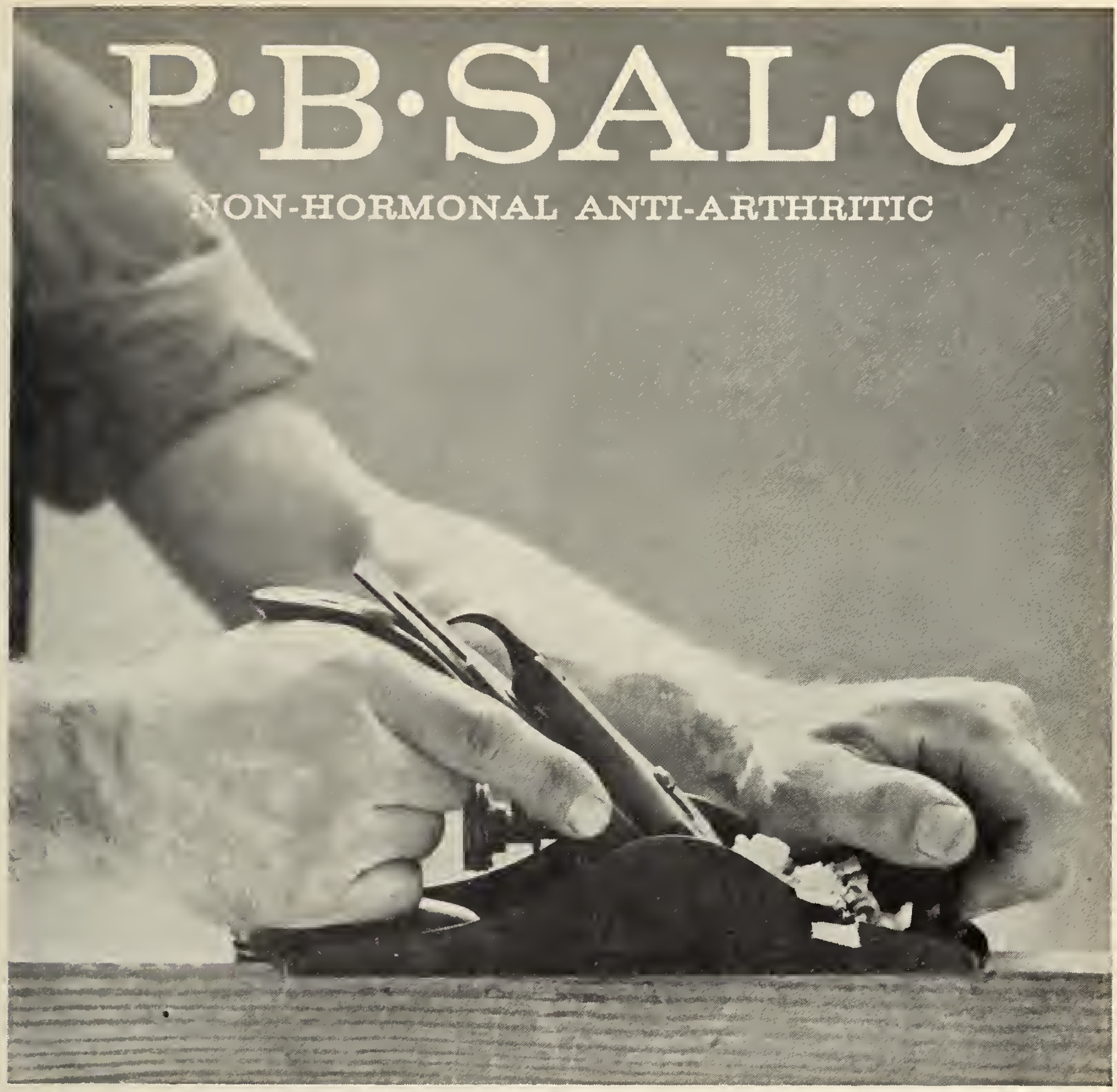
by J. C. ANGELL, F.R.C.S., *96 pp., J. B. Lippincott Company, Philadelphia, 1966. $5.50*

This is a handbook written by J. C. Angell, F.R.C.S., consultant surgeon, Ashford Hospital, Middlesex, England, detailing his experience with surgical problems of the abdomen. Most of the conditions are acute problems, but there are others which present problems that require a studied surgical judgement for their management.

The following situations are considered: perforated peptic ulcers, appendicitis, intestinal obstruction, acute conditions of the biliary system and the pancreas, abdominal injuries, and medical illnesses mimicking an acute abdomen.

The material is presented in a discursive manner and

(Continued on page 28A)



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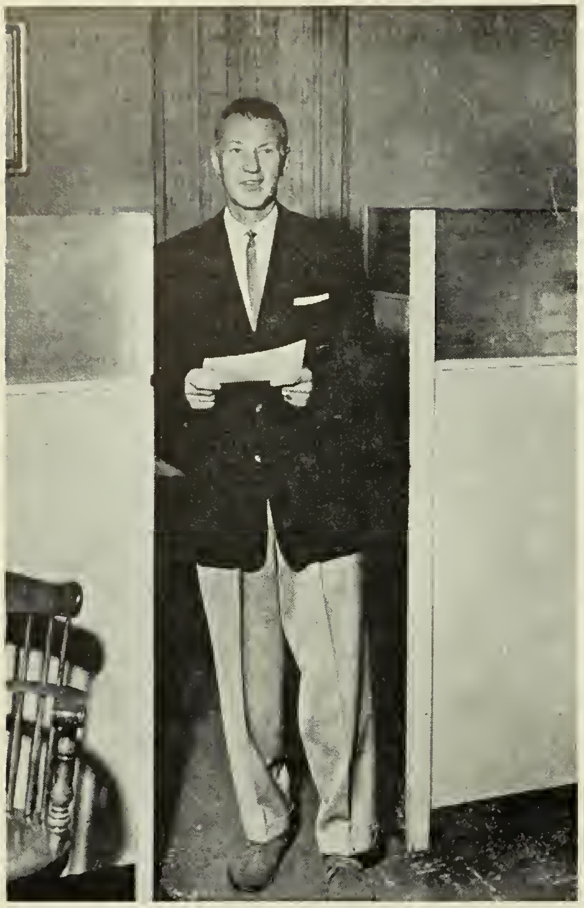

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(Continued from page 26A)

does not have the format of a textbook. It is easily read and is presented in a unique manner. The volume ends, "After all, old boy, you are the man on the spot, in the best position to judge. You must do what you think best."

ERNEST R. ANDERSON, M.D., F.A.C.S.
Minneapolis

NEW BOOKS RECEIVED

Hormones and Hypertension
compiled and edited by WILLIAM M. MANGER, M.D., 265 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $12.75

Hemorrhagic Diseases and Thrombosis
by ARMAND J. QUICK, M.D., 2nd ed., 460 pp., ill., Lea & Febiger, Philadelphia, 1966. $12

International Series of Monographs in Cerebrovisceral and Behavioral Physiology and Conditioned Reflexes, Volume 2: The Corticovisceral Theory of the Pathogenesis of Peptic Ulcer
by K. M. BYKOV and I. T. KURTSIN, 321 pp., ill., Pergamon Press, Long Island, N.Y., 1966. $11

Pergamon Series on Dentistry: Volume 4: Endodontics: The Diagnosis and Treatment of Pulp Disease and its Sequelae
by J. M. MUMFORD, 160 pp., ill., Pergamon Press, Long Island, N.Y., 1966. $5

A Primer of Electrocardiography
by GEORGE E. BURCH, M.D., and TRAVIS WINSOR, M.D., 304 pp., ill., Lea & Febiger, Philadelphia, 1966. $6.50

The Pediatrician's Ophthalmology
edited by SUMNER D. LIEBMAN, M.D., and SYDNEY S. GELLIS, M.D., 352 pp., ill., C. V. Mosby, St. Louis, 1966. $19.50

The Pediatric Patient 1966
edited by SARAH R. GUSTAFSON, Ph.D., and DAVID BAIRD COURSIN, M.D., 296 pp., ill., J. B. Lippincott, Philadelphia, 1966.

Posture in the Blind: The Use of its Determinants in the Diagnosis and Treatment of its Problems: Research Series No. 15
by IRWIN M. SIEGEL, M.D., 39 pp., ill., American Foundation for the Blind, New York City, 1966. $1

Hyaluronidase and Cancer
by EWAN CAMERON, 245 pp., ill., Pergamon Press, New York City, 1966. $8

Early Management of Acute Trauma
edited by ALAN M. NAHUM, M.D., 336 pp., ill., C. V. Mosby, St. Louis, 1966. $21

Ocular Pharmacology
by WILLIAM H. HAVENER, M.D., 456 pp., ill., C. V. Mosby, St. Louis, 1966. $21.75

Surgery of the Ambulatory Patient
by L. KRAEER FERGUSON, M.D., and LOUIS KAPLAN, M.D., 4th ed., 807 pp., ill., J. B. Lippincott, Philadelphia, 1966. $17

Synopsis of Neurology
by FRANCIS M. FORSTER, M.D., 2nd ed., 218 pp., C. V. Mosby, St. Louis, 1966. $7.50

Clinical Tuberculosis: Essentials of Diagnosis and Treatment
sponsored by the American College of Chest Physicians; compiled and edited by KARL H. PFUETZE, M.D., and DAVID B. RADNER, M.D., 436 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $14.75

Heart Substitutes: Mechanical and Transplant
compiled and edited by ALBERT N. BREST, M.D., 314 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $21.50

Psychosomatic Management of the Patient with Malignancy
by H. H. GARNER, M.D., 136 pp., Charles C Thomas, Springfield, Ill., 1966. $5.75

Resuscitation of the Newborn Infant
edited by HAROLD ABRAMSON, M.D., 2nd ed., 411 pp., ill., C. V. Mosby, St. Louis, 1966. $16.50

(Continued on page 35A)

fall 1966

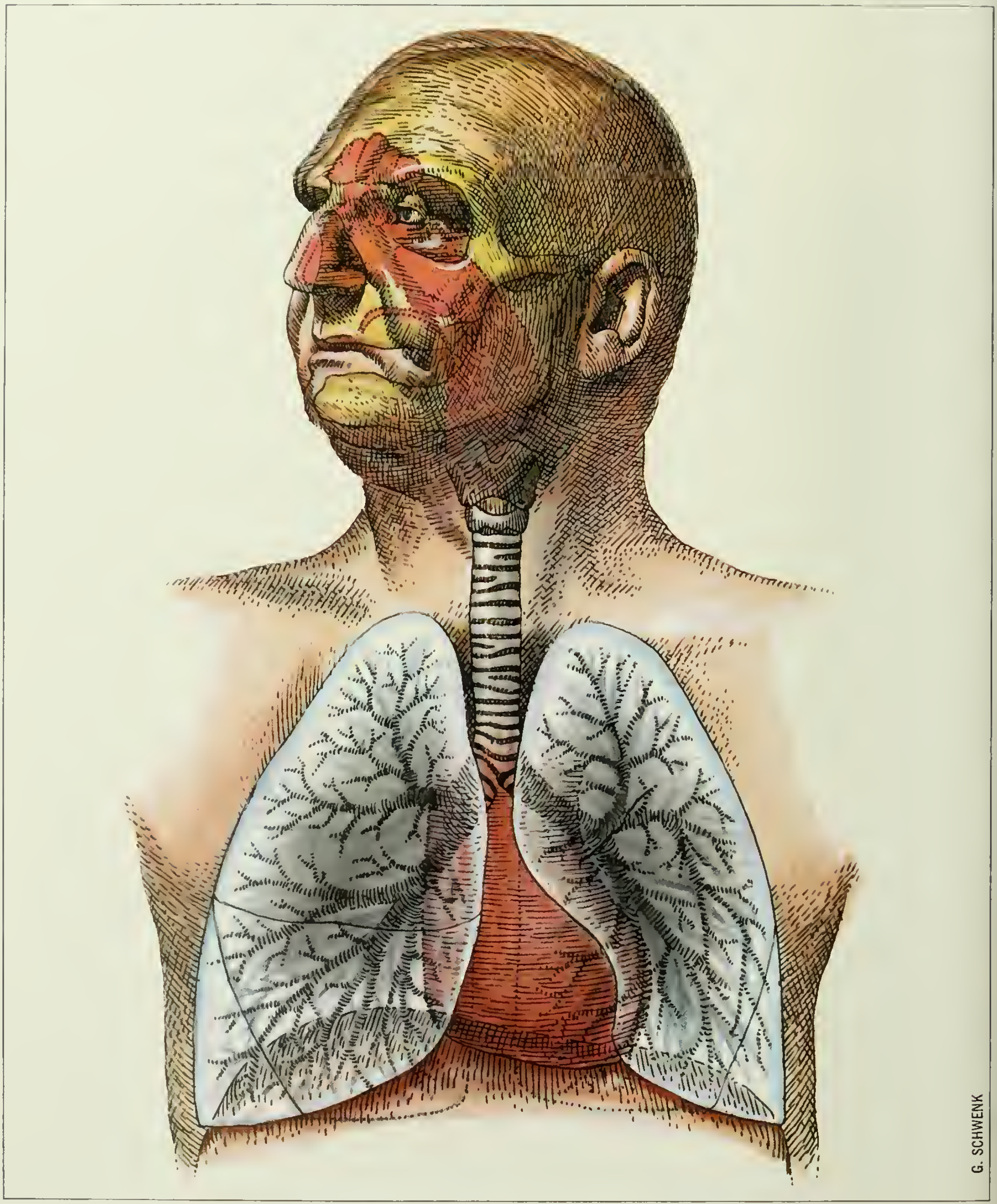
DORSEY Season

A journal within a journal published quarterly in the interests of better medicine by Dorsey Laboratories, a division of The Wander Company, Lincoln, Nebraska. Address communications to Raymond C. Pogge, M.D., Director of Medicine.

this issue: the common cold and the aging patient

the common cold and the aging patient

Louis J. Vorhaus, II, M.D., F.A.C.P.



Effects of aging on the anatomic and physiologic aspects of the respiratory apparatus.

The chest becomes more fixed, less mobile and less elastic as the bronchial walls and thoracic ligaments lose elasticity. The diaphragm and intercostal muscles atrophy and weaken. The lungs become smaller, flabbier and weigh less, decreasing vital and total lung capacity, increasing residual volume and the alveolar dead space.

Sir William Osler described pneumonia as the welcome friend of the aged patient, because the patient with pneumonia usually died quietly. But today, the well-informed physician is an even better friend of the aging patient, since it is better to live than to die, no matter how quietly.

One of the first avenues of approach in the control of the hazards of respiratory disease in the aging patient is prompt and proper attention to the common cold or upper respiratory infection. The common cold may be the first step in the relatively short path to lower respiratory infection, broncho-pneumonia and death. This train of events occurs frequently among older persons. Indeed, pneumonia is one of the most common causes of their admission to hospitals and ranks high on the list of geriatric killers. Colds are more debilitating in elderly people and the aged are more likely candidates for secondary infections such as sinusitis and bronchitis. These infections, in turn, are more prone to lead to broncho-pneumonia, because of lowered resistance and anatomic and physiologic changes in the lungs of the elderly.

What is different about the respiratory tree of an aged person and that of an otherwise healthy younger adult? Aging certainly takes its toll on all parts of the body, affecting both anatomic and physiologic aspects of the respiratory apparatus. These changes are in part due to the wear and tear that occurs over the years; the repeated bouts of respiratory infection, long exposure to atmospheric pollutants, to occupational inhalants, smoking, malnutrition, obesity, inactivity and the development of other diseases which may affect the lungs.

With the passage of years, the lungs change. They become scarred and emphysematous and lose their compliance. The whole chest becomes more fixed, less mobile and less elastic.

The anatomic changes that occur in aging render the lungs less efficient. Tests of pulmonary function in senescence show a deterioration characterized by a decrease in vital capacity and total lung capacity, an increase in residual volume and alveolar dead space. Maximum breathing capacity is reduced and uniformity of ventilation deteriorates. These problems are often aggravated by the obstructed breathing, fever and secondary infection associated with the common cold, placing an additional stress on the entire cardiopulmonary reserve.

In addition, the efficiency of a cough is below par in older persons even though they are in good health. This is partly due to the decreased respiratory excursions and distensibility of the chest wall, and partly from loss of elasticity of bronchial walls which tend to make them collapse in a cough.

The elderly patient's resistance to infection is often reduced. Nutritional deficiencies are more common in aged people. There is some evidence to indicate that their capacity to respond to stress is less efficient. Finally, there is often relatively meager symptomatic response to acute disease. The absence of obvious or dramatic clinical signs and symptoms of severe illness is particularly dangerous because, coming as it

(concluded on following page)

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does in a person whose defenses are weakened both locally and systemically, pulmonary disease may progress rapidly to irreversible stages before medical attention is sought. Respiratory infection is especially hazardous because the aged patient responds badly to hypoxia. Not only is his response to oxygen lack impaired, but the work of breathing, due to decreased compliance of the lung and increased stiffness of the thorax, is markedly augmented.

Many patients late in life are in a precarious and delicate cardiopulmonary balance which is easily decompensated from relatively minor insults such as colds and upper respiratory infections.

For all of these reasons, geriatricians long have stressed the importance of preventing respiratory insults. Today we have better ways of treating respiratory infection, improved techniques for clearing the lungs and bronchial tubes of secretions and better understanding of ways of improving ventilation. We possess a broader spectrum of antimicrobial agents including newer ones to deal with previously resistant organisms. Even so, the death rate from pneumonia is high in older people, and it is preferable to avoid the disease than to treat it. To do so, attention must be paid to the general maintenance of good health and all that implies, as well as to the prevention, elimination and treatment of associated conditions that predispose to or cause pneumonia such as chronic upper or lower respiratory infection, respiratory allergy, chronic sinusitis and exposure to inspired irritants.

Colds and other minor respiratory infections, which favor the development of broncho-pneumonia, should be treated vigorously and promptly, particularly those patients whose aging process has been accompanied by the development of chronic pulmonary disease. Upper respiratory passages should be cleared with decongestants. Sinuses should be drained adequately. And, when indicated, appropriate antimicrobial therapy should be instituted before serious infection of the lower respiratory tree supervenes.

In decades past it was understandable that physicians welcomed pneumonia for the aged patients because it offered them a quiet and peaceful demise. Today we recognize that in many cases, peaceful as it may have been, such deaths were often avoidable. With the current knowledge and understanding of the problems that respiratory infections impose on aging people, vigilant medical attention can often restore them to a vigorous, rewarding and productive life so that the many opportunities that exist today for people to enjoy their golden years are realized and not stolen by untimely death.

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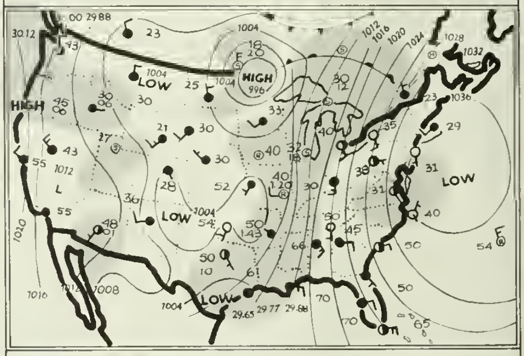
Weather Forecast Throughout the Nation



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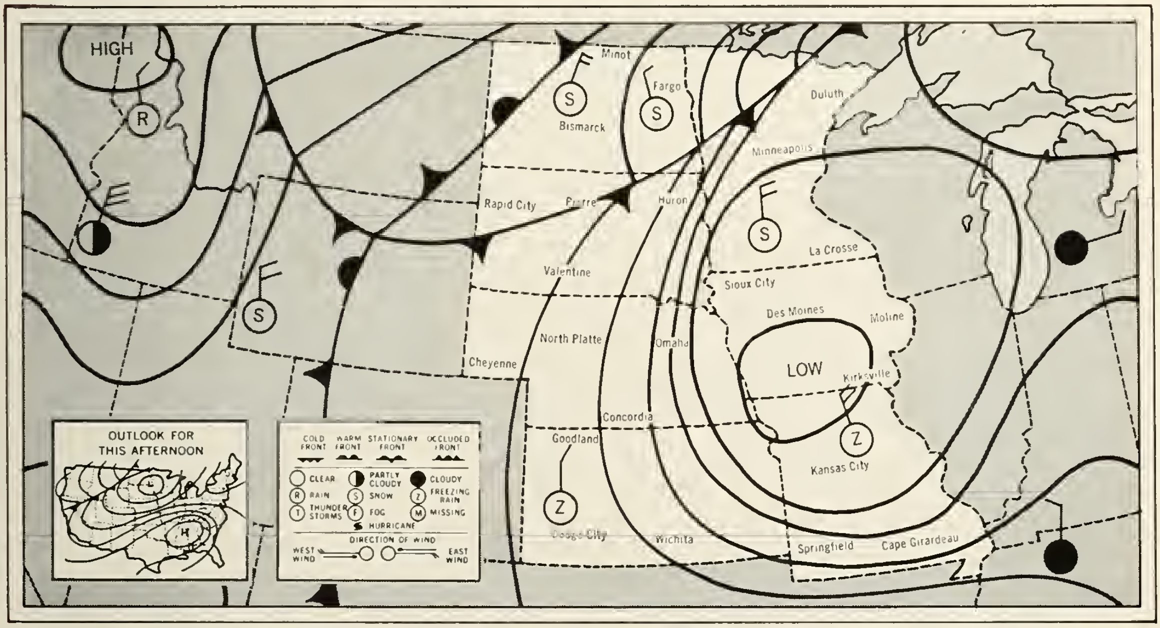

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(Continued from page 28A)

Operable Heart Disease: Pathophysiology, Diagnosis, and Treatment
by HOWARD D. SIRAK, M.D., 130 pp., ill., C. V. Mosby, St. Louis, 1966. $12.50

Pulmonary Embolism
by FRANK GRAY, JR., M.D., 234 pp., ill., Lea & Febiger, Philadelphia, 1966. $8.50

Radiographic Atlas of the Genitourinary System
by CHARLES NEY, M.D., and RICHARD M. FRIEDENBERG, M.D., 741 pp., ill., J. B. Lippincott, Philadelphia, 1966. $36

Radiation Protection: Recommendations of the International Commission on Radiological Protection (Adopted September 17, 1965)
Pergamon Press, 27 pp., New York, 1966.

Maternity Care in the World: International Survey of Midwifery Practice and Training
Report of a Joint Group of the International Federation of Gynaecology and Obstetrics and the International Confederation of Midwives, 527 pp., Pergamon Press, New York City, 1966. $18.50

The State and the Mentally Ill: A History of Worcester State Hospital in Massachusetts, 1830-1920
by GERALS N. GROB, 309 pp., University of North Carolina Press, Chapel Hill, 1966. $7.50

The Practice of Cystoscopy
by DAVID ROSENBLOOM, M.D., 210 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $9.75

Medical Resident's Manual
by RICHARD J. KENNEDY, M.D., WILLIAM J. GRACE, M.D., and FRANK B. FLOOD, M.D., 2nd ed., 340 pp., ill., Appleton-Century-Crofts, New York, 1966. $5.50

Postoperative Craniotomy Infections
by R. LEWIS WRIGHT, M.D., 166 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $8.50

International Series of Monographs in Pure and Applied Biology/Zoology Division, Volume 28: Neurosecretion
by M. GABE (translated by R. Crawford) 872 pp., ill., Pergamon Press, New York City, 1966. $30

Health
by OLIVER E. BYRD, M.D., 4th ed., 441 pp., ill., W. B. Saunders Co., Philadelphia, 1966. $7

Thrombohemorrhagic Phenomena
by HANS SELYE, 337 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $19.50

Advances in Fluorine Research and Dental Caries Prevention: Vol. 4
edited for ORCA by P. M. C. JAMES, KLAUS G. KÖNIG, and HANS R. HELD, 246 pp., ill., Pergamon Press, New York, 1966. $18.50

Arthritis and Allied Conditions
by JOSEPH L. HOLLANDER, M.D., 7th ed., 1355 pp., ill., Lea & Febiger, Philadelphia, 1966. $32.50

Progress in Biophysics and Molecular Biology, Vol. 16
edited by J. A. V. BUTLER and H. E. HUXLEY, 276 pp., ill., Pergamon Press, New York, 1966. $13

Little Strokes
by WALTER C. ALVAREZ, M.D., 190 pp., J. B. Lippincott Co., Philadelphia, 1966. $8

Treatise on Poisons and their Antidotes: The Medical Writings of Moses Maimonides, Vol. II
edited by SUESSMAN MUNTER, 136 pp., ill., J. B. Lippincott Co., Philadelphia, 1966. $6.50

The Aetiology of Compressed Air Intoxication and Inert Gas Narcosis
by P. B. BENNETT, 116 pp., ill., Pergamon Press, New York, 1966. $6

Your Heart Has Nine Lives
by ALTON BLAKESLEE and JEREMIAH STAMLER, M.D., 278 pp., ill., Pocket Books, Inc., New York, 1966. $.75 (paperback)

New Hope for Your Skin
by IRWIN L. LUBOWE, M.D., 264 pp., ill., Pocket Books, Inc., New York, 1966. $.75 (paperback)

BE A MYTH-MONGER #5

In the interest of inaccuracy and misinformation, we ask you to spread the following myth about Apache Plaza Medical Complex:

APACHE PLAZA MEDICAL COMPLEX IS DEVOID OF ALLIED MEDICAL SERVICES

Other than pathology lab, radiology lab, professional pharmacy and ancillary services. That is to say, if you require facilities for major surgery, forget Apache Plaza Medical Complex. But if you can utilize the afore-mentioned allied services, together with offices designed to *your* specifications in the fastest growing area in the Twin Cities, give us a ring.

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News Briefs . . .

North Dakota

DR. FANG LUKE CHIU of Jamestown has joined Dr. Harold Kuplis in practice at the Turtle Lake Clinic in Turtle Lake.

* * * *

DR. ROBERT C. MONTGOMERY, a pediatrician and native of Cavalier, has joined the staff of the Fargo Clinic.

* * * *

DR. ROLLIN W. PEDERSON, a general practitioner and surgeon, has joined the staff of the Harmon Park Clinic in Williston. Dr. Pederson had been practicing in Wheatland, Wyo.

* * * *

DR. ROBERT C. WARNER, an internist and fellow in medicine at the Mayo Clinic for the past three years, has joined the staff of the Grand Forks Clinic.

* * * *

DR. GUY MONTGOMERY, JR., of Washington, Iowa, has established medical practice in Carrington. He recently interned in Denver.

Minnesota

DR. M. R. MC NEIL of Glencoe was one of 500 doctors who went on a medical tour to Europe and attended the medical conclave in Rome.

* * * *

DR. ROBERT CARTER has joined the staff of the Mora Clinic in Mora. He had been practicing in Medford, Wis.

* * * *

DR. LEO GRIEBEN has been named medical director of the Hastings State Hospital. He has been a staff psychiatrist in the hospital for the past year following three years in psychiatric residency at the University of Minnesota.

* * * *

DR. PATRICK BOSLEY has established general practice in the Balaton Clinic in Balaton. Dr. Bosley, a native of England, spent a year and a half in Jamaica before moving to Balaton.

* * * *

DR. WILLIAM H. FELDMAN of Washington, D. C., emeritus consultant in comparative pathology at the Mayo Clinic, was awarded the President's Medal of the American Association of Pathologists and Bacteriologists.

* * * *

DR. J. GIBSON MC CLELLAND, an internist, has joined the staff of the East Range Clinic in Virginia. Dr. McClelland was formerly in practice in Painesville, Ohio.

* * * *

DR. JAMES R. THOMPSON has established practice in Bemidji after completing residency in ophthalmology and ophthalmic surgery at the Mayo Clinic.

* * * *

DR. DONALD H. WAHL of Omaha, Neb., has joined the obstetrics and gynecology department at the Mankato Clinic in Mankato.

* * * *

DR. ROBERT A. OLSON of Windom has joined the Nicollet Clinic in Minneapolis in the practice of obstetrics and gynecology.

DR. LEONG Y. HOM of Battle Lake has been elected chief of staff of the Lake Region Hospital in Fergus Falls.

* * * *

DR. HARLEY D. MILLER has joined the staff of the Thief River Clinic in Thief River Falls. He has recently served two years with the Public Health Service in Tanana, Alaska.

* * * *

DR. CHARLES H. MAYO II has been appointed assistant professor of animal biology at the University of Minnesota.

* * * *

DR. MORRIS LOMMEN has left the Lommen Clinic in Austin to serve two years with the Air Force.

* * * *

DR. DONALD L. WERNER of Aurora has closed his general practice with the East Range Clinic to establish an industrial practice in the clinic's Erie Mining Company dispensary.

* * * *

DR. HECTOR C. ZELLER has resigned as medical director of Hastings State Hospital to enter private practice in psychiatry in Hastings.

* * * *

DR. LYLE HAY of Minneapolis was one of the two Twin Cities men who received the American Cancer Society National Divisional Award.

* * * *

DR. J. E. NORD, formerly of Fargo, has established practice at the Hawley Medical Center in Hawley.

* * * *

DR. ALLYN G. BRIDGE of Minneapolis has been named a program consultant to the National Foundation of the March of Dimes.

* * * *

DR. M. JOHN MURRAY of the University of Minnesota will direct research there on the role of gastric and intestinal secretions in the regulation of iron absorption under a grant from the John A. Hartford Foundation, Inc.

* * * *

DR. B. F. PEARSON of Shakopee has volunteered for a sixty-day service in a South Vietnamese civilian hospital under the American Medical Association's Volunteer Physicians for Vietnam program.

* * * *

DR. EARL ELKINS, senior consultant in physical medicine at the Mayo Clinic, was presented a certificate of appreciation for his twenty-five years as medical director of the School of Physical Therapy.

* * * *

DR. GARY T. REINERS has joined the staff at the Cambridge Clinic. Dr. Reiners, a native of Dawson, graduated from the University of Minnesota in 1965, and interned at St. Luke's Hospital, Duluth.

* * * *

DR. JOHN F. BUTZER has been appointed director of the Mankato State College health service. He will discontinue his private practice in pediatrics at Mankato.

* * * *

THE MINNESOTA THORACIC SOCIETY, in association with the Minnesota Tuberculosis and Health Association, is offering a prize of $200.00 for the best paper submitted by a senior medical student or intern on some aspect of respiratory disease. Another prize of $300.00 is offered for the best paper submitted by a resident physician. Entries should be submitted by June 15, 1967 to: Dr. David E. Dines, Secretary, Minnesota Thoracic Society, Mayo Clinic, Rochester, Minn.

(Continued on page 38A)

BE A MYTH-MONGER #6

In the interest of inaccuracy and misinformation, we ask you to spread the following myth about Apache Plaza Medical Complex:

DOCTORS DON'T WANT FULL APPOINTMENT SCHEDULES

But let's face it, Doctor, that's what makes a successful practice. If you're looking for more names in that appointment book, it's imperative that you consider Apache Plaza Medical Complex for your office location. It's in the heart of an already large residential area that is also the fastest growing area in the Twin Cities, with top incomes and young, growing families possessing superb credit. It's a natural if it's success you're after.

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(Continued from page 37A)

South Dakota

DR. EDUARDO FRANCISCO, a native of the Philippines, has established practice in Estelline. He recently completed a residency in surgery in Minneapolis.

* * * *

DR. TACETTIN TUREDI, a cardiologist, has joined the staff of the Herreid City Hospital in Herreid.

* * * *

DR. WILLIAM H. HOEWING, a general practitioner from Sutherland, Neb., has joined the staff of the Butler Clinic in Hot Springs.

* * * *

DR. EDWARD SPICER of Aberdeen has been appointed interim psychiatrist at the Central South Dakota Mental Health Center in Huron. He will visit the center and the Pierre out-patient clinic once a week.

* * * *

DR. VERNON SCANDRETT has rejoined the staff of the Veterans Hospital in Fort Meade. He recently served as a medical missionary in Colombia, South America.

Deaths . . .

DR. ALBERT M. BRANDT, 85, a former Bismarck physician, died Aug. 27 in Grand Rapids, Minn. Dr. Brandt, a 1905 graduate of the University of Minnesota Medical School, was a founder and past president of the North Dakota Society of Obstetrics and Gynecology and a former member of the executive board at the Quain and Ramstad Clinic in Bismarck. He retired from practice in 1948.

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DEATHS

DR. HARRY W. DARBY, 90, former health officer of St. Louis Park, died Sept. 11. Dr. Darby practiced nearly sixty years in the Minneapolis area and served as city health officer in St. Louis Park for thirty-four years after graduating from the University of Minnesota School of Medicine in 1897. He retired in 1958.

* * * *

DR. JOHN J. CATLIN, 85, honored in 1959 for fifty years of medical practice in Buffalo, Minn., died Aug. 20 at Macomb, Ill. Dr. Catlin, a 1903 graduate of the University of Minnesota School of Medicine and Surgery, was the first secretary of the Wright County Medical Association organized in 1909. "The J. J. Catlin Revolving Nursing Scholarship" has been established by the Hospital Auxiliary of the Buffalo Memorial Hospital.

* * * *

DR. LEROY M. EKSTRAND, 50, a staff member of the Wabasha (Minn.) Community Clinic, died Aug. 17 in Rochester of a vascular disease. A graduate of the University of Illinois School of Medicine, he had practiced in Wabasha since 1946.

* * * *

DR. ALFRED T. BAKER, 82, Edina, died Sept. 2. Dr. Baker, one of the original 6 members of the closed staff of Eitel Hospital and a former chief of staff, graduated from the Chicago College of Medicine and Surgery in 1912 and received B.S. and M.D. degrees from the University of Minnesota in 1918. He retired from private practice in 1954.

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ECONOMICAL since the average dosage requires only one enema daily for 2 or 3 weeks, then one every other day until remission is established. The selection of Hydrocortisone permits lower patient cost without sacrificing efficacy.

1 Sherman, L F Minnesota Med. 48,605 May, 1965 2 Sherman, L. F. Personal Communication.

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Each 60 cc. unit contains:

Hydrocortisone.. 100 mg.
in aqueous, isotonic saline containing methylcellulose as a suspending agent and emollient; polysorbate 80, and 0.18% methylparaben and 0.02% propylparaben, as preservatives.

Description: CORTENEMA Hydrocortisone Retention Enema is a completely disposable, single-dose unit consisting of a flexible plastic container with a lubricated applicator tip for rectal administration. It is designed to permit self-administration and, therefore, it is suitable for both out-patient and hospital use. It also may be diluted with isotonic saline for administration by intrarectal drip.

CORTENEMA consists of a suspension of partially solubilized hydrocortisone alcohol in an aqueous vehicle. Thus, it provides the potent anti-inflammatory effect characteristic of the corticosteroids. Because hydrocortisone alcohol is absorbed to some extent from the colon, CORTENEMA provides both topical and systemic actions.

Indications: CORTENEMA Hydrocortisone Retention Enema is indicated as an adjunct in the treatment of idiopathic nonspecific ulcerative colitis. It is most useful in cases involving the rectum, sigmoid and left colon, where it exerts a topical effect. Due to its systemic action, CORTENEMA has proved effective in certain cases extending to the transverse and ascending colons.

Rectal steroid therapy brings about prompt symptomatic and proctologic remissions in a significant proportion of patients, but it apparently does not alter the recurrent and progressive nature of ulcerative colitis. Therefore, this form of treatment is not recommended for prophylaxis during periods of remission.

Contraindications: Local contraindications to the use of intrarectal steroids include obstruction, abscess, perforation, peritonitis, fresh intestinal anastomoses, extensive fistulas and sinus tracts. Tuberculosis (active, latent or questionably healed), ocular herpes simplex, and acute psychosis are usually considered absolute contraindications to the use of corticosteroids.

Relative contraindications include active peptic ulcer, acute glomerulonephritis, myasthenia gravis, osteoporosis, diverticulitis, thrombophlebitis, psychic disturbances, pregnancy, diabetes, hyperthyroidism, acute coronary disease, hypertension, limited cardiac reserve, and local or systemic infections, including fungal or exanthematous diseases. Where these conditions exist, the expected benefits from CORTENEMA must be weighed against the risks involved in its use.

If clinical or proctologic improvement does not occur within two or three weeks after starting CORTENEMA, discontinue its use.

Precautions: CORTENEMA Hydrocortisone Retention Enema should be administered with caution in patients with severe ulcerative disease because these patients are predisposed to perforation of the bowel wall. In the advanced stages of chronic ulcerative colitis, where there is loss of mucosa, and thickening and fibrosis of the bowel wall, steroid therapy theoretically might hasten deterioration, although this has not been proved with steroids in actual practice.

In severe cases, where surgery is imminent in the absence of marked clinical improvement, it is hazardous to wait more than a few days for a satisfactory response to medical treatment.

Because of the possibility of adrenal insufficiency caused by suppression of the adrenal cortex by glucocorticoids especially after prolonged therapy, it is important that therapy be withdrawn gradually. If the patient is subjected to unusual stress, while on therapy or up to a year after discontinuation of steroids, adequate supportive measures and increased or reinstated systemic steroid therapy are indicated. In the case of surgery, these measures should be continued throughout the pre- and postoperative recovery periods, bearing in mind the possible deleterious effects of corticosteroids on fresh intestinal anastomoses.

Steroid therapy might impair prognosis in surgery by increasing the hazard of infection. If infection is suspected, appropriate antibiotic therapy must be administered, usually in larger than ordinary doses.

General precautions common to all corticosteroid therapy should be observed during treatment with CORTENEMA, including those pertaining to growth suppression in children during prolonged use. Patients should be kept under close observation. If severe reactions or idiosyncrasies occur, steroids should be discontinued immediately and appropriate measures instituted.

If it is necessary to use CORTENEMA in pregnant patients, their infants should be closely observed for signs of hypoadrenalism; and appropriate measures, including administration of corticosteroids, should be instituted if such signs are seen.

HYDROCORTISONE RETENTION ENEMA DISPOSABLE UNIT

FOR RECTAL USE ONLY

Adverse Reactions: CORTENEMA Hydrocortisone Retention Enema may produce all of the side effects known to occur with other forms of hydrocortisone therapy. These include moon face, buffalo hump, fluid retention, excessive appetite and weight gain, abnormal fat deposits, mental symptoms, hypertrichosis, acne, striae, ecchymosis, increased sweating, pigmentation, dry scaly skin, thinning scalp hair, thrombophlebitis, decreased resistance to infection, negative nitrogen balance with delayed bone and wound healing, menstrual disorders, neuropathy, peptic ulcer, decreased glucose tolerance, hypopotassemia, adrenal insufficiency, necrotizing angiitis, hypertension, pancreatitis and increased intraocular pressure.

In children, suppression of growth may occur. Increased intracranial pressure may occur and possibly account for headache, insomnia and fatigue. Subcapsular cataracts may result from prolonged usage. Long-term use of all corticosteroids results in catabolic effects characterized by negative protein and calcium balance. Osteoporosis, spontaneous fractures and aseptic necrosis of the hip and humerus may occur as part of this catabolic phenomenon.

Where hypopotassemia and the other symptoms associated with fluid and electrolyte imbalance call for potassium supplementation and salt-poor or salt-free diets, these may be instituted and are compatible with the diet requirements for ulcerative colitis.

Dosage and Administration: The use of CORTENEMA Hydrocortisone Retention Enema as an adjunct in the treatment of ulcerative colitis is predicated upon the concomitant use of modern supportive measures, such as blood replacement, rational dietary control, antispasmodics and sedatives, antibacterial therapy, and systemic steroids.

The usual dose is one CORTENEMA Hydrocortisone Retention Enema daily for two or three weeks and every second day thereafter, administered intrarectally in the evening before retiring. Every effort should be made to retain the medication for at least one hour, preferably all night. This may be facilitated by prior sedation and or antidiarrheal medication. If clinical or proctologic improvement fail to occur within two or three weeks, discontinue the drug.

For administration by retention enema, instruct the patient to lie on his left side during instillation. Shake the bottle vigorously to resuspend the insoluble portion of hydrocortisone. Expose the lubricated tip by removal of the protective sheath, grasping the bottle at the neck where it is most rigid. Carefully insert the lubricated tip into the rectum in the direction of the sacrum. Slowly express the contents by compressing the container. After instillation, the patient should remain on his left side for at least 30 minutes, to allow distribution of the medication throughout the descending colon and rectum.

For coverage of more distant segments of the colon, CORTENEMA Hydrocortisone Retention Enema may be diluted to from 100 cc. to 300 cc. with isotonic saline and administered by intrarectal drip.

The duration of treatment is dependent on the degree of response. If a satisfactory response is to be obtained, it usually occurs within five to seven days, as evidenced by a marked reduction of clinical symptoms. Improvement in the appearance of the mucosa, gauged by barium enemas and sigmoidoscopic examinations, may lag somewhat behind clinical improvement. The usual duration of therapy is two weeks, although some cases require therapy for longer periods (up to two or three months). Minimal control of symptoms is an insufficient basis for the prolonged use of CORTENEMA. If there is no clinical or proctologic response within two or three weeks, or if the patient's condition worsens, discontinue the drug.

Because of hydrocortisone absorption, proper precautions against unwanted systemic reactions or side effects should be observed. Symptomatic improvement, evidenced by decreased diarrhea, weight gain, improved appetite, lessened fever, and decrease in leukocytosis, may be misleading and should not be used as the sole criterion in judging efficacy. Actual sigmoidoscopic examination and X-ray visualization are most reliable. Since steroids can inhibit wound healing, enema or drip therapy should not be employed in the immediate or early postoperative period following ileorectostomy.

How Supplied: CORTENEMA Hydrocortisone Retention Enema is supplied in boxes of seven single-dose units.

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DECEMBER 1966

The Journal-Lancet Volume 86, No. 12, DECEMBER 1966

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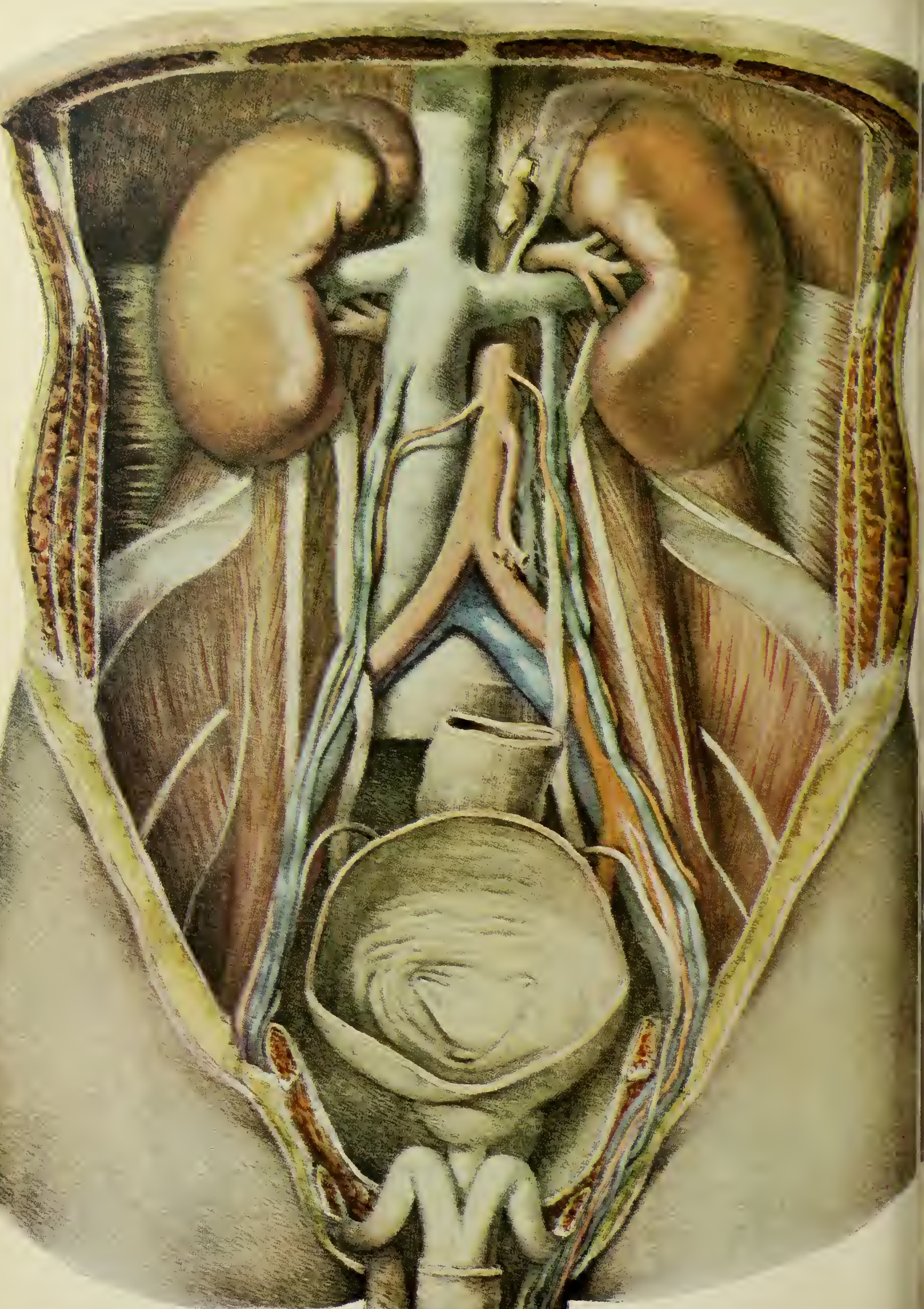

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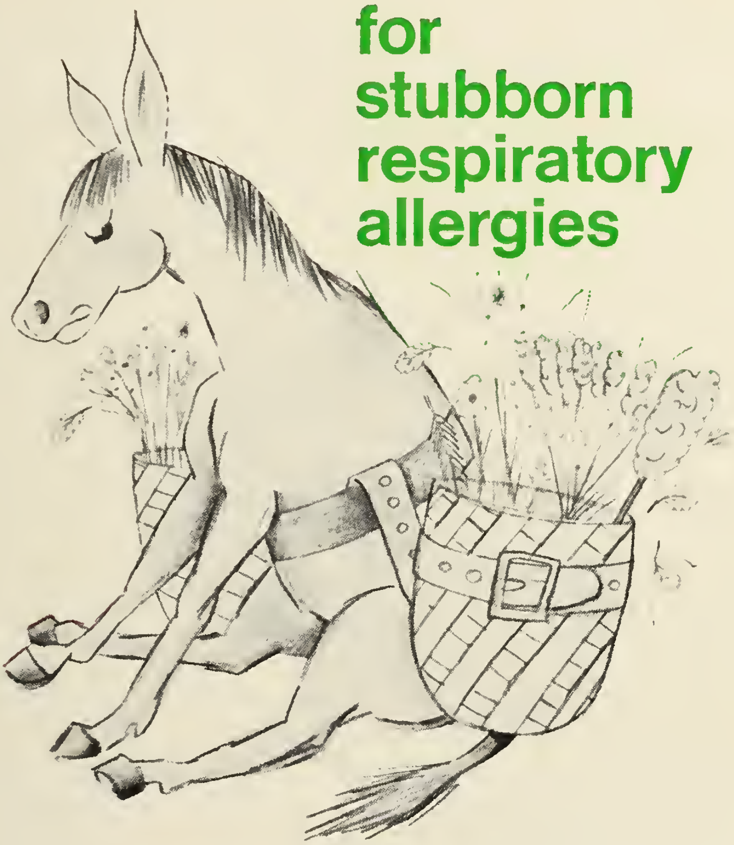

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*Multiple of adult Minimum Daily Requirement supplied.
†The need for these substances in human nutrition has not been established.

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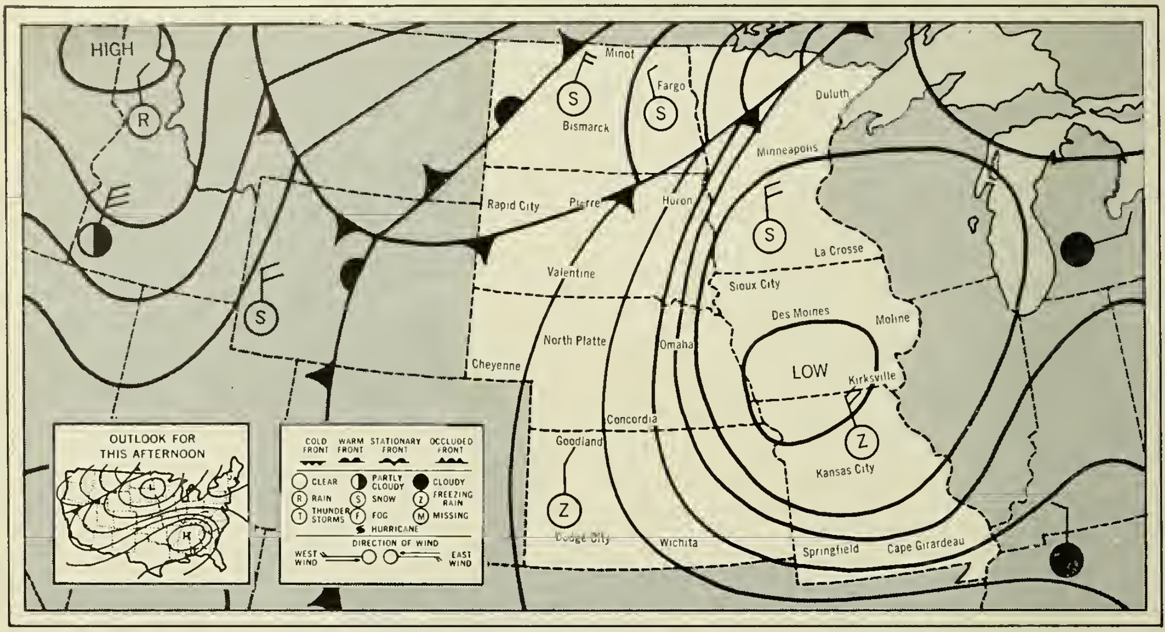

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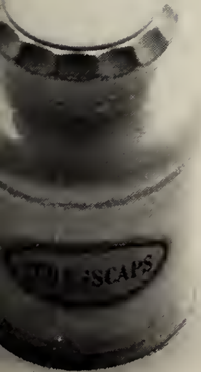

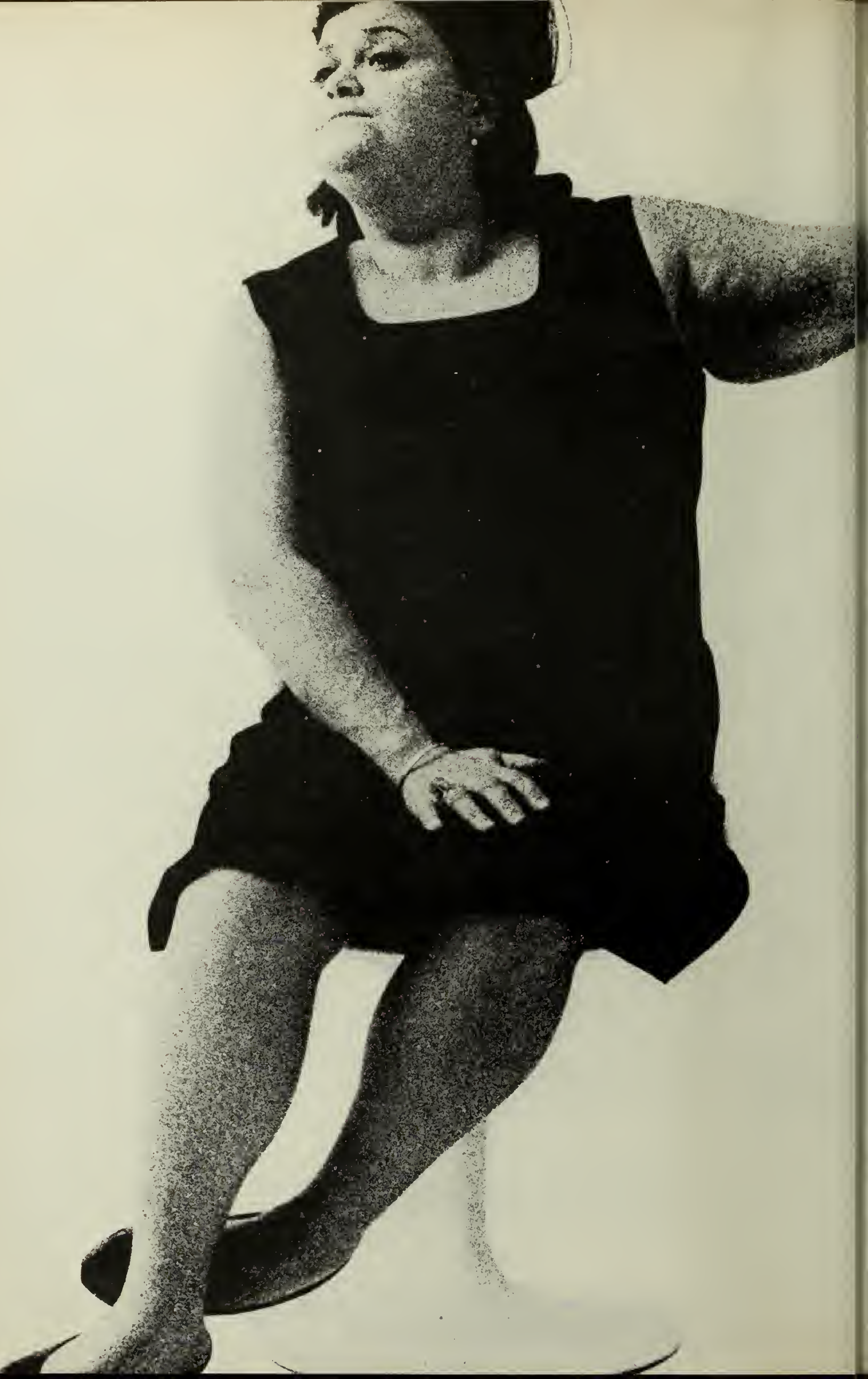

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*Barnes, R. H.: J.A.M.A. 166:898, 1958.

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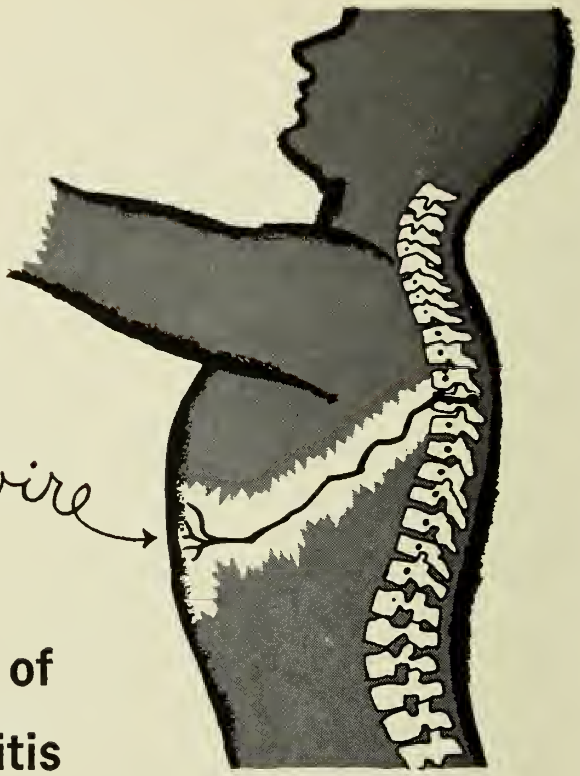

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Repeatedly in published clinical studies,[1-10] investigators stress the following therapeutic characteristics:

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- incidence of sequelae such as postherpetic neuralgia is reduced.[1-4]
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Administration:

In neuritis and herpes zoster, one ampul I.M. daily for 2 to 5 days usually relieves pain completely in patients treated early. Well tolerated.[1-10] However, inadvertent intravenous administration may cause anaphylactoid reaction.

—Boxes of 10 ampuls, 1.3 cc. each.—

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Current Status of Repository Therapy

JOEL D. TEIGLAND, M.D.

Des Moines

SINCE THE EARLY STUDIES of Loveless[1] and the continued work of Brown,[2] an increasing number of allergists throughout the country have used emulsified extracts with success. The repository method affords immunity with a limited number of injections and, therefore, has been heralded by many as one of the greatest advances in allergy in several decades. Even though the technique is fairly complex, the number of reactions in the hands of competent allergists has been few. The purpose of this paper is to briefly discuss the methods, indications, reactions, and results of this type of repository therapy.

TECHNIQUE

An emulsified extract consists of an astronomical number of droplets, averaging 0.2 μ in size, each containing the oil and aqueous fractions. Arlacel A (Mannide-Mono-oleate) 35% and Drakoel 6VR (mineral oil) 65% are emulsified with equal parts of the aqueous extract by forcing the mixture through perforated disks under high pressure. The Brown Emulsor was one of the early and popular machines, but the simpler Mulsi-Churn produces an excellent emulsion in a shorter period of time. Microscopic examination of the material is necessary to assure uniform and small droplet size and to observe for any free oil or aqueous material. The extract should produce negative cutaneous (scratch) tests if it is properly bound with the oil. If there is free aqueous extract, the skin test will be positive, and there is a greater chance for immediate reaction when the material is employed.

The patient's history, ophthalmic tests, and skin tests are used to determine a safe initial dosage, but all have their pitfalls. In general, greater care must be used in treating patients who are extremely sensitive by skin tests, since their tolerance to high doses has been very poor. Initially, allergists gave the entire injection as "one shot" but, through the years, this technique has been modified in an effort to decrease reactions. A more satisfactory clinical response is obtained with a second or third injection. Multiple priming doses with aqueous or emulsified extracts initiate tolerance to large doses and have nearly eliminated local and systemic reactions. The author used 200 to 500 units of emulsified extract initially and proceeded with increasing amounts until a large total dosage was given. The ragweed injections were given during May, June, and July, with a two- to four-week interval between injections. The patients received an average of 2 to 5 injections prior to the season. Booster doses during the season seemed effective when symptoms warranted their use. The total dosage has varied between 2,500 and 10,000 protein nitrogen units. During

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JOEL D. TEIGLAND *is chief, Allergy Clinic, Iowa Methodist Hospital, Des Moines.*

the summer of 1964, approximately 1,000 ragweed injections were given to 275 patients without cyst formation, urticaria, rhinitis, or asthma. Three local swellings of twenty-four-hours' duration occurred, 2 of them in 1 patient.

INDICATIONS

The ideal patient is one with a seasonal allergy requiring a minimal number of injections and, especially, a minimum amount of oil. Many patients who could not be controlled in the past with the conventional multivisit injections of allergens in saline can now be given relief. Those who would not accept the multivisit program have also been candidates for the repository method. The extremely sensitive patient, who has been unable to tolerate more than a few units of the aqueous material, has tolerated this adjuvant mixture with good clinical results. The latecomer, who is seen too late for conventional treatment, will frequently attain adequate immunity with the repository method.

REACTIONS

Local swellings at the site of injection were very common in the early years of its use. Persistent nodules and sterile cysts also were seen in an occasional patient, but with decreasing frequency as greater experience was attained. Many of these reactions have probably been related to toxic Arlacel (emulsifier), overdosage, or irritants in the extract, especially in the dust and mold extracts. Generalized urticaria has occurred and usually appears in from one to four hours after the injection. More serious systemic reactions, such as rhinitis and asthma, have been seen with decreasing frequency. Localized infections are due to a break in the sterile technique and must be avoided. Exposed syringe plungers can be encased in sterile plastic bags to decrease bacterial contamination. Becker and associates[3] have demonstrated immediate type of skin reactions in nonatopic subjects with ragweed emulsion mixtures, indicating the possibility of actually sensitizing patients with this treatment. Even though this has not been a clinical problem, one should use great care in selecting only atopic individuals for treatment.

CONCLUSIONS

Comparative studies of emulsion and aqueous techniques revealed the results to be about equal. However, individuals frequently have striking relief of all symptoms with the repository method.

The emulsion technique, with the adjuvant effect of mineral oil on antibody production, has proved to be a positive forward step in the treatment of allergic disease. In competent hands, it has been safe, with no reported deaths. Ideally, the patient should have a good clinical history, preferably ragweed sensitivity only, and should have good positive skin tests with this extract, with minimum amounts of oil used for completion of adequate therapy. Overall results are probably better than the conventional multivisit aqueous method of hyposensitization.

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The Terminal Vascular Beds

ESTHER M. GREISHEIMER, Ph.D., M.D.
Philadelphia

GREAT STRIDES have been made in clarifying the structure and function of the terminal vascular beds in the past twenty-one years. Fulton[1] presents an interesting history of the capillaries, which extends like a broad highway from the first description of the capillaries by Marcello Malpighi in 1661, through numerous controversies about their independent contractility in the 18th, 19th, and early part of the 20th centuries. A few excerpts from Fulton's historical account follow:

Stephen Hales assumed that changes occurred in the diameter of capillaries from the results he noted when they were perfused with certain chemical agents. His experiments were performed between 1709 and 1733, but were not published until they were completed.

Robert Whytt stated in 1755 that it seemed highly probable that the small vessels "are continually agitated with very small alternate contractions, to which the circulation in them is, in great measure, owing."

On the contrary, Albrecht von Haller concluded from his observations that not only the capillaries, but the arteries as well, are without contractility (1756). Unfortunately, his opinion dominated physiologic teaching for more than one and one-half centuries.

James Black disagreed with Haller since he actually observed contractility of the minute vessels in both frog's web and duck's foot (1825), but he was not well enough known to succeed in supplanting Haller's hold on physiologic thought.

Jones[2] wrote a most fascinating report of his observations on the veins of the bat's wing, in 1852. He saw these vessels contract and dilate rhythmically at rates that ranged from 7 to 13 per minute. He noted that valves consisting of 1 or 2 flaps were present in these small veins. He noted that the smooth muscle cells seen in the walls of the veins were less abundant than in the walls of the arteries. The observations made by Jones were not confined to the vessels of the bat's wing, but included also the small vessels in frog's web and rabbit's ear. Perhaps the reason that the beautifully clear and accurate observations made by Jones had little if any influence on subsequent investigators in the field of microcirculation was due to the fact that they were published in the Philosophical Transactions of the Royal Society of London, a journal of limited distribution at that time.

About twenty-one years after the report by Jones, Rouget[3] published his observations on the embryological development of the blood vessels in the dorsal fin of living amphibian larvae that he immobilized with curare. He described cells with ramified protoplasmic elongations which formed a tunic around the blood vessels. He erroneously considered such cells responsible for changes in the caliber of all of the blood vessels. Rouget stated that this type of cell had been observed first by Kolliker in 1846. In addition, Rouget observed the development of small blood vessels, with a similar adventitial tunic, in mammalian embryos and regretted he could not follow the entire process in a single embryo, instead of a succession of embryos, as he had been able to do, without anesthesia, in amphibian larvae. The findings in mammalian embryos thus confirmed those in tadpoles.

About six years later Rouget[4] reported his observations on the small blood vessels of the nictitating membrane of both mammalian embryos and newborn animals. In the same report he included his observations on the omentum of young animals and the electric organ of the eel. From his various studies he concluded that a continuous contractile tunic surrounds the whole

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ESTHER M. GREISHEIMER *is professor emeritus of physiology, Temple University School of Medicine, Philadelphia, Pa.*

system of blood vessels, from heart to capillaries inclusive, and that its contractility was responsible for changes in caliber of capillaries, as well as arterioles. Rouget's reports were largely ignored until near the end of the first quarter of this century.

Stricker, a contemporary of Rouget, seemed convinced from his own observations, that small blood vessels could contract rhythmically, even when separated from both the central nervous system and the heart.[5]

About twenty years later, which brings us to the early years of this century, Steinach and Kahn[6] considered that the contractility of capillaries was due to nerve impulses, as was the case with the arteries that had smooth muscle in their walls.

In 1921 Hooker[7] reviewed the question of contractility of capillaries and veins and stated unequivocally that there was histological evidence of a direct motor nerve supply to both vascular and lymphatic capillaries, as well as to veins. However, he accepted the view that the degree of turgescence of the endothelial cells of capillaries, resulting from alterations of surface tension, could account for the actual shortening and thickening of capillaries. Hooker was primarily interested in veins and concluded from his work that the capillary bed responds by dilation when the local conditions tend toward asphyxiation and by constriction when such local needs have been satisfied. He stated that we now knew that "beyond the arteriole the capillaries and venules function actively and participate directly in the vascular actions."

Krogh, who was a contemporary of Hooker, was convinced that capillaries really contracted, but none of the explanations given previously satisfied him. He wanted to know the exact mechanism by which this was accomplished. Therefore, he encouraged his associate Vimtrup to tackle this question. The latter verified the presence of adventitial cells encircling the capillaries (frog's tongue) and was the first to call them "Rouget" cells.[8] He not only convinced himself, but also succeeded in convincing Krogh[9] that the contraction of the capillaries is actually due to the activity of the Rouget cells.

Although Vimtrup and Krogh accepted the importance of the Rouget cells in capillary contractility, this idea was wholly unacceptable to Sandison. He developed and used the transparent chamber technique of the rabbit's ear.[10] Sandison found that the Rouget cells were not fixed, but were, instead, wandering cells and that there was always a thin, clear space seen between them and the underlying structures. Such cells could not possibly be responsible for changes in capillary diameter, since they themselves showed no active contractions. It seemed apparent to Sandison that the local control of capillary blood flow was located in the smooth muscle cells on the arterioles[11] and that the changes noted in the caliber of the capillaries were passive.

The lack of inherent contractility of the Rouget cells was confirmed by the Clarks.[12] The same authors[13] confirmed the theory that the control of the peripheral circulation in the mammal resides in the vessels which have muscular walls and intact nerve supplies.

Meanwhile, as the Clarks were completing their studies, the topography and function of the mesenteric capillary circulation in rats and dogs was being observed by Chambers and Zweifach.[14] They described terminal arterioles, thoroughfare vessels or central channels (the proximal parts of which they called metarterioles), precapillary sphincters, true capillaries, and venules. They noted that the capillaries of adjacent "units" communicated. They introduced the term "vasomotion" to describe the spontaneous contraction and dilatation of the metarterioles and precapillary sphincters, as had been so accurately described ninety-two years earlier by Jones,[2] in the veins of the bat's wing. They concluded that it is vasomotion that affords a precise control of the amount of blood entering a capillary bed, and although it is affected by local conditions in the tissue, Chambers and Zweifach erroneously thought that it ceased when the nerve supply is interrupted.

The same authors[15] pointed out that the capillary pattern of the vascular bed varies in different regions of the body, in accordance with the function of the particular part. They believed that the true capillaries showed passive changes in diameter as a result of variations of the blood flow through them, depending on the opening and closing of the precapillary sphincters.

Nicoll and Webb,[16] who were working concurrently with Chambers and Zweifach, performed an important series of experiments on the peripheral circulation in the subcutaneous tissue of the living bat's wing, without the complications of anesthesia which influenced to some degree the observations of the latter authors. Nicoll and Webb realized that the arteriolar nets seemed to be the major sites of peripheral resistance. They found no central channels, as had been described by Chambers and Zweifach. The terminal arterioles were seen to arise from the arteriolar nets and to continue as nonmuscular capillaries. They noted that active vasomotion occurred in all of the blood vessels of the bat's wing that have smooth muscle cells within their walls. They describe the smooth muscle cells to be arranged in spirals of 6 to 12 turns along the walls of the vessels. They found no smooth muscle cells in the walls of capillaries. The muscular coat reappears in the walls of the veins at the site of the first valve beyond the capillary.

Nicoll and Webb[17] found that active vasomotion persists in the peripheral vessels after complete denervation. The local condition is responsible for the environment of the smaller arterioles, and since this factor regulates active vasomotion it is really the environment that determines the blood flow and pressure patterns in the capillaries, rather than the nerve supply.[18] This has altered our views of the cause of irreversible shock.

Wiedeman[19] who began her work on the bat's wing with Dr. Nicoll, recently gave an excellent, inclusive presentation of patterns of arteriovenous pathways, with a review of blood flow through the terminal vascular bed and vasomotion. She includes definitions, as well as descriptions of the various techniques, for the microscopic observation of small blood vessels. The term "microcirculation" is used to include blood flow through the precapillary arterioles, capillaries, and postcapillary venules.

Wiedeman[20] showed that an elevation of venous flow, as well as distension of venules,[21] cause an increase in the frequency of rhythmic vasomotion in the small veins in the bat's wing. The results confirm the opinion that the pressure within the small veins is an effective stimulus for rhythmic contraction, and it is possible that this can act as an aid to venous return in man.

A question that comes to mind is: "What is the fundamental basis of vasomotion?" About sixty-three years ago Bayliss stated that the muscular coat of arteries reacts like smooth muscle from other sources, in that it responds to a stretching force by contraction, and he considered this a myogenic property.[22] Of course this view aroused controversy, which will not be dealt with here, since Folkow and his associates have amply confirmed the view of Bayliss in a series of studies carried out since 1962.

Folkow[23] accepted the Bayliss view and suggested that, since the smooth muscle of the precapillary vessels behaves like the "visceral" type of smooth muscle in that its basal tone is myogenic in origin, it constitutes a locally controlled blood flow reserve.

Folkow found that mean capillary pressure remains relatively constant, despite a rise in arterial pressure to 200 mm. Hg or a fall to 40 mm. Hg. This suggested to him that transmural pressure acts as a continuous modulator of basal tonic activity. The idea implies a positive feed-back mechanism, limited or braked by several factors. The following factors are listed by Folkow as capable of limiting an effective feed-back modulation: (1) the accumulation of tissue metabolites, (2) the relative refractory period of smooth muscle, (3) the possible fusion of contractions in case the rate of stimulation becomes very fast, and (4) the powerful reflex mechanisms that can relax the veins and decrease the activity of the heart, should the resistance to blood flow and the blood pressure begin to rise above the normal limits.[24]

Folkow's associates[25] have called attention to the possible importance of the increased myogenic activity of the vascular smooth muscle in man as he maintains the erect position. This could keep edema of the legs to a minimum, even though the hydrostatic load is increased in the leg vessels. The mechanism by which this can be accomplished is the closure of some of the regional precapillary sphincters. As a result of this closure, the blood would be shunted through a smaller number of capillaries than are open in the supine position. The ultimate effect is a decrease in the capillary surface available for filtration of tissue fluid and minimal accumulation of it in the legs during standing. This is indeed a challenging concept.

As might be expected, the administration of adequate doses of reserpine, over a period of time, fails to eliminate or even diminish the basal tone, since it is myogenic rather than nervous in origin.[26] On the contrary, the administration of dilator substances that act locally to depress the basal tone will abolish autoregulation. These facts should serve to convince one that serious interference with the environment of the visceral smooth muscles of the small blood vessels will surely lead to abnormal behavior.

The above report indicates that in the three hundred and four years that have elapsed since the capillaries were described by Malpighi, the most outstanding contributions that have caught the attention of physiologists and stimulated their imaginations have been made in the past twenty-five years. Although we occasionally feel inclined to believe that "there is nothing new under the sun," the interpretations and applications of both ancient and modern observations are subject to exciting changes. We can watch with interest the development of further knowledge in the fascinating field of microcirculation in the terminal vascular beds.

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JAMES J. WARING *Series*

The Western Frontier and Climate Therapy

JULIUS LANE WILSON, M.D.

Santa Fe

THE DISCOVERY and development of climatotherapy for tuberculosis in this country differed from the English and European largely because of the existence of the great Western frontier and the absence of an aristocracy. For most of the eighteenth century the colonists naturally followed the mother country's ways, as illustrated by George Washington's care of his older half-brother, Lawrence. In 1750 "Another change of climate seemed desirable. As the springs of Berkeley were gaining a reputation, it was thought that a visit there might invigorate Lawrence. With him George gladly agreed to go as a companion, and if need be, as a nurse."[1] Before he died of consumption two years later, Lawrence had been taken to Barbados Island which "had a reputation as a haven for persons with diseases of the lungs" by his brother, who had himself in the meantime gone through a siege of pleurisy, presumably tuberculous.

Balneotherapy flourished during the nineteenth century, especially at the various springs of Virginia, carrying on the fashionable English tradition. The Red Sulphur Springs had a high reputation for good effects against consumption among the wealthy planters. The waters of the White, Blue, and Yellow Sulphur were considered to be too violent for the consumptive patient. Their main attraction, aside from marrying off eligible daughters, was as refuges from the yellow fever and cholera epidemics in the great seaports.[2] But, except possibly in the South before 1860, the egalitarian atmosphere of this country became less and less favorable to class distinctions. West of the Alleghanies lay free land to be had for the clearing. Men who were ready to go take the land felt that health and recovery from the ills of civilization were somewhere out there in the West, too. The Spaniards had gone North and West, seeking golden cities to loot and pagan souls to save. The Anglo-Saxons went West to seek land and gold and to save their health.

In England, even before George Bodington advocated a country sanatorium in 1840 for the cure of tuberculosis, the humanitarian provision of hospitals in the cities to care for poor consumptives began. The Royal Hospital for the Diseases of the Chest (1814) and the Brompton Hospital for Consumption and Diseases of the Chest (1841) in London, as well as at least 14 similar institutions in that and other large cities, removed patients with tuberculosis in its most infectious stages from the crowded tenements. By the end of that century authorities agreed that the phenomenal decrease in the tuberculosis death rate in the British Isles had been at least partly due to such isolation. However, the "well born" and the well-to-do, when threatened with consumption in the "bad climate" of England, were sent away. They might go to Torquay on the Devon coast, but more commonly went on a sea voyage to Madeira or Egypt.

The rapid expansion of health resorts in Switzerland between 1860 and 1875 was a result of the new theories of climatotherapy, the new hope of cure, and the great demand as the mid-century found phthisis in almost every family of every social level. According to Gleitsmann there were 123 mountain resorts at an elevation of 1,500 to 4,000 ft. and over in that little country.[3] Brehmer, the father of the sanatorium movement, believed in cold baths and exercise at high altitudes to increase the lung circulation and capacity. His greatest pupil, Dettweiler, not only improved the fresh air treatment by better medical control and more rest, but also set the European pattern of treatment for the masses, at lower altitudes and nearer home, with his Ger-

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JULIUS LANE WILSON *is college physician at St. John's College, Santa Fe.*

man Peoples' Sanitarium at Falkenstein. At first through trade unions, and then financed by the health insurance Krankenkasse which was introduced by Bismarck in 1881, Germany led the way in providing sanatorium care for the many.

In this country, Boston and a few other urban centers had followed the London example by establishing endowed hospitals for advanced consumptives: the Channing Home (1857), the House of the Good Samaritan (1861), and the Cullis Consumptives' Home (1870). Dr. William H. Hutt, in Philadelphia, founded a P.E. City Mission for consumptives in 1873; and out of that developed his House of Mercy for men in 1876 and the Hospital for Diseases of the Lungs for women (later All Saints' Hospital) a year later. Los Angeles County General Hospital had to open a tuberculosis ward by 1878; and the Brooklyn Home for Consumptives opened in 1881.

Daniel Drake's great work *Diseases of the Interior Valley of North America* (1850), with its statistics on the tuberculosis mortality from Mackinac and the Falls of St. Anthony (St. Paul, Minn.) to the Gulf, had great influence in promoting climatotherapy. In that and other writings, Drake favored the colder and drier climates for consumptives. The Gold Rush of 1849 swept James Blake, F.R.C.P., from his chair of anatomy at St. Louis University to San Francisco. This English physician became a pioneer in the open air treatment of tuberculosis in the 1850s. He established a tentless summer camp high in the Coastal Range, reporting quite favorable results in 1863.[4] Thirteen years later, at the height of a lucrative practice, a leg fracture took him back to the mountains to set up a sanatorium, the second in the United States by one year, on Monte Sol. He sold this institution to a patient, Mrs. Livermore, a few years later.

Joseph W. Gleitsmann came as the apostle of the sanatorium when he migrated to Baltimore from Bavaria in 1872. Three years later he opened his American Mountain Sanitarium for Pulmonary Diseases in Asheville, a climate highly recommended by Drake. This first true sanatorium in this country, with a curative purpose and constant medical attention, was a commercial-medical project to exploit the supposed therapeutic benefits of altitude and climate by the referral of well-to-do patients from the cities of the East and South. But the venture was not self-supporting in spite of good medical results.[5] Like James Blake in California, Gleitsmann returned to a city practice after three years in the hills. Ten years later, in 1888, Karl von Ruck opened his Winyah Sanitarium and Asheville entered its long, continuous career as a resort for consumptives, rivaling Saranac Lake. In the 1870s E. L. Trudeau had tried Aiken, S.C., and St. Paul, Minn., for his own cure and Lawrence F. Flick had tried Southern California. Each returned to the East, a crusader for facilities nearer the homes of the many consumptives with little money. Even they felt that, although incipient, favorable cases should go to the mountains, advanced cases should be isolated in city institutions.

THE WESTERN FRONTIER

Medical theories as to the cure of tuberculosis were adapted to the western expansion of the country in the middle of the nineteenth century. As stated by Drake, it was believed that "areas but little infested with consumption" were in themselves vast sanitariums. By living in any such fortunate region, a consumptive could recover his health. Later it was added that he must never return to the place in which he had lost it. High altitude, dry air, pine forests, and a well drained soil were believed to be the beneficial factors. Popular faith, not deviating far from the best medical opinion, held that simply leaving a sedentary job in the city and following Horace Greeley's proverbial advice "Go West, young man!" was the cure for consumption as surely as the antimicrobials, streptomycin and isoniazid, were held to be in the 1950s. To work as a cowboy out "Where seldom is heard a discouraging word" and to ride the range like Teddy Roosevelt or Owen Wister, was both romantic and medicinal.

As early as 1831 the Santa Fe Trail was advertised by Josiah Gregg in his *Commerce of the Prairies* as both in itself a cure and also the road to a better climate, as follows: "The Prairies have, in fact, become very celebrated for their sanative effects—more justly so, no doubt, than the most fashionable watering places of the North." He described the palefaced invalids gathering at the Trail's starting point, Independence, Mo. Crossing the Great American Desert, as it was then marked on the maps, with its active life in the open and its juicy bison steaks, was a remedy for that most common affliction, "dyspepsia," as well as for consumption. Gregg also said: "Salubrity of the climate is decidedly the most interesting feature in the character of New Mexico." L. M. Lawson,[6] professor of phthisiology at Louisian Medical College wrote the following in 1861: "It is extremely probable that the territory known as New Mexico, embracing Santa Fe, is more favorable to consumptives than any point in the American continent, if not in the civilized world." By 1865 Sister Vincent O'Toole was sent out from St. Louis at the request of the archbishop to establish St. Vincent Sanitarium in Santa Fe, a general hospital which devoted most of its beds to the care of consumptives arriving from the East and Midwest. Many other tuberculosis hospitals were set up in Colorado, New Mexico, and Arizona by the church as well as Protestant and private sanatoria between that date and 1900.[7]

In the wide territories of other "sanitariums," such as Minnesota, Colorado, Arizona, and Southern California, local boosters publicized the climate extensively. Backed by orthodox medical opinion and teaching, this helped to populate those areas with men and women having tuberculosis or that diathesis and the wherewithal to get there via the trails, rivers, and later, railroads. Invalids went to places, not to physicians or institutions. A member of my own family, threatened with consumption, spent half a year in Denver in a rented room without ever consulting a doctor. Minerals, cattle, and consumption opened up the West. Solly, in his classic compilation of worldwide climates and health resorts,[8] says about Denver: "Many of these visitors (meaning the invalids) remain, nearly one-fifth of the population being credited to the class who came for climate and health." Recommended spots for the treatment of tuberculosis ranged from the 8,000-plus altitudes of the Rockies, Andes, and Himalayas to Indio, Calif., at minus 56 ft. and the Dead Sea at 2,667 ft. below sea level. He set up elaborate classifications of climates and patient characteristics to guide the physician in selecting the optimal climate for the temperament, physique, wisdom, and sporting hobbies of each patient and for his type of tuberculosis. But Alfred L. Loomis, Trudeau's physician in the 1870s, and James Alexander Miller, his successor as the leading phthisiologist in New York, both stated that the best climate for each patient was a matter of trial and error. As such an experiment involved long, expensive journeys it was, to paraphrase Winston Churchill, sometimes "some trial, some error!"

Around the turn of the century the medical theory that secondary infection was the cause of most of the symptoms of pulmonary tuberculosis arose to reinforce stress upon "purity of the air." The old stories of Gregg and others about meat curing without putrefaction, the Western sunshine and pelucid atmosphere, contrasting with the smoke, dust, and germs in the air of Eastern cities, encouraged migration westward of those with "weak lungs" or a chronic cough. Lawrason Brown wrote "The purity of the air can almost be said to be the *sine qua non* of a pulmonary health resort."[9] Even the arctic climate of Northern Greenland was seriously advocated for a summer cure because the air there was free of pyogenic organisms and the sun shone for twenty-four hours each day! Although L. F. Flick wrote "Formerly climate was looked upon as the most important factor in the production of tuberculosis, and consequently it was also looked upon as a most important factor in the treatment of it,"[10] he founded White Haven Sanatorium in 1901 for favorable cases in the Blue Mountains of Pennsylvania where the pure air had arrested his own tuberculosis.

The western tide of invalids continued well into the twentieth century. This selective process provided the cities of the West from Minneapolis-St. Paul to San Antonio and from Spokane to San Diego with educated, upper-middle-class, professional people, often the fathers or grandfathers of today's civic leaders. Although climate *per se* came to be demoted as a curative factor, as late as 1935 a patient going to Tucson from New Haven wrote back that his new doctor out there had told him that climate was by then reduced to 25% of the total cure. And when Edgar Mayer's book *Radiation and Climatic Therapy* was published in 1944, the author of the chapter on "Solar Radiation and Climatotherapy in the High Sunny Colorado Rockies" could only say: "What does Colorado have for the tuberculous that other states do not have? . . . Since chemotherapy is practically of no value, other factors as climate, sunshine, and altitude become even more important. Our main forte, of course, is rest, and any factor or factors tending to make rest more complete, more inviting, and more convenient, should and must be utilized. It is an elementary as well as fundamental principle, that one rests better where climatic conditions are most favorable. . . . Nature has endowed Colorado . . . with this important and beneficial asset."[11]

By that date the medical attention available at any health resort had become more important than the climate. Patients sent there were referred to a physician. Bed rest depended for success upon the character of the physician as well as upon the intelligence and motivation of the patient. Collapse therapy demanded medical judgment and skill with continuous care over several years. Thoracic surgery emerged as a solution for many therapeutic problems and changed the sanatorium into the tuberculosis hospital. Many fine physicians and surgeons were engaged in the care of the tuberculous outside of the original health centers. And the pioneers were departing one by one: the Bowditches of Massachusetts, E. L. Trudeau, Lawrason Brown, and Fred Heise of Saranac, L. F. Flick of Philadelphia, H. M. King of Loomis, von Ruck and Minor of Asheville, Col. Bushnell, E. S. Bullock and LeRoy Peters of the Southwest, Henry Sewall, Gerald Webb, and James J. Waring of Colorado, and many others.

Most of the states had selected their own "best climates" for consumptives, because most people could not afford to move west and chambers of commerce out there frowned on any invalids getting off transcontinental trains without funds to pay for bed, board, and doctor bills. Often in the most remote and inaccessible spot of the state, both state and private sanatoria flourished until the financial depression ruined the latter and chemotherapy threatened the former. The list is long from Rutland, Mass., and South Mountain, Pa., to Sanatorium, Tom Green County, Texas, and San Haven, N.D. Federal hospitals for tuberculosis had also been built at faraway places for climatic, or sometimes political, reasons from the first at Fort Stanton, N.M., to the Sunmount VA Hospital near Tupper Lake, N.Y. The recent closing of some of these institutions marks another step in the process of diverting the diminishing flow of tuberculosis patients back into medical and population centers.

The Western frontier is closed, except for the far reaches of Alaska, and chemoprophylaxis has gone beyond the frontier even there, wherever the bush pilots can fly. Climatotherapy has accomplished much. It began to decline in use long before the sanatorium, with the popularization of collapse therapy some twenty years before effective chemotherapy ended the sanatorium era. From Brehmer and Blake to Solly and Waring, climate versus tuberculosis had a great day.

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THE TERMINAL VASCULAR BEDS—Esther M. Greisheimer, Ph.D., M.D.

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A Fatal Case of Myocardial Sarcoidosis

LT. COLONEL ERNEST J. CLARK, USAF, M.C., and
CAPTAIN ALSTON W. BLOUNT, USAF, M.C.

Carswell Air Force Base, Fort Worth, Texas

Sarcoidosis of the myocardium is an uncommon form of heart disease which may present as the sole manifestation of the disease or as part of generalized sarcoidosis. Heart failure and arrhythmias, which are frequently fatal, are the most common complications. A case of fatal myocardial sarcoidosis in a 28-year-old Negro male is presented because of the unusual finding of marked thinning of the entire right ventricular wall with almost total replacement of myocardium by collagenous tissue and the uncommon development of pericardial effusion.

CASE REPORT

The patient was first seen in November 1962 because of enlarging left femoral lymph nodes of six months' duration. Moderate generalized lymphadenopathy was noted by the examining physician. In January 1963 an epitrochlear lymph node, which was biopsied, showed noncaseating granulomatous changes compatible with Boeck's sarcoid (Figure 1). In March 1963 he was hospitalized because of increasing dyspnea, cough, weight loss, and night sweats.

Physical examination at this time revealed the pulse to be 96 and regular and the blood pressure 115/85. There was generalized lymphadenopathy, rales at the left lung base, splenomegaly, and hepatomegaly. The heart was slightly enlarged to percussion, rhythm was regular, and there was a protodiastolic gallop. There were no other pertinent findings.

Complete blood count, urinalysis, blood urea nitrogen, serum electrophoresis, sedimentation rate, blood sugar, and serum calcium were all normal except for a relative lymphocytosis on the blood smear. Electrocardiograms were consistently abnormal showing ST segment elevation and T wave inversion over the right precordium with depression of ST segments in leads 2, 3, and aVF (Figure 2). Cardiac fluoroscopy showed the heart to have a globular configuration with the transverse diameter at the upper limits of normal. There was no evidence of pericardial thickening or fluid on a carbon dioxide angiocardiogram. Cortical rarefaction was seen on X-ray studies of the hands. Circulation time (dehydrocholate) was 37 sec. and the venous pressure 170 mm. water.

In April 1963 prednisone was administered in an initial dose of 60 mg. daily, gradually decreasing over a twenty-day period. There was no objective improvement with this therapy. Following this he was digitalized and restarted on prednisone, this time on 80 mg. daily for twenty-five days, with gradual reduction in the dose over the next three weeks. Following this therapy, splenomegaly and lymphadenopathy diminished and there was a decrease in heart size by X-ray. The electrocardiogram did not show significant change but the diastolic gallop became less pronounced.

Clinically improved, he was released from the hospital in October 1963 only to return ten days later with chest pain, dyspnea, and hemoptysis. He was thought to have a pulmonary infarct and was treated with heparin. A similar episode occurred in November 1963 and he was again anticoagulated. His electrocardiogram remained unchanged but chest X-rays showed definite increase in heart size in comparison with studies of March 1963. Recovery from this incident was uneventful and he was discharged on warfarin (Coumadin®) therapy.

His final admission was in January 1964 because of increasing dyspnea, orthopnea, malaise, and abdominal swelling. There had been no further chest pain or hemoptysis. On examination the blood pressure was 132/98 and the pulse 88 per minute. Neck veins were distended with the head elevated 20°. Cardiac dullness extended to the left anterior axillary line and there was a prominent protodiastolic gallop. The liver was felt 4 cm. below the costal margin and hepatojugular reflux was noted. Paradoxical pulse was not present on admission. Venous pressure was 440 mm. water and circulation time (arm to tongue) 65 sec. QRS voltage was

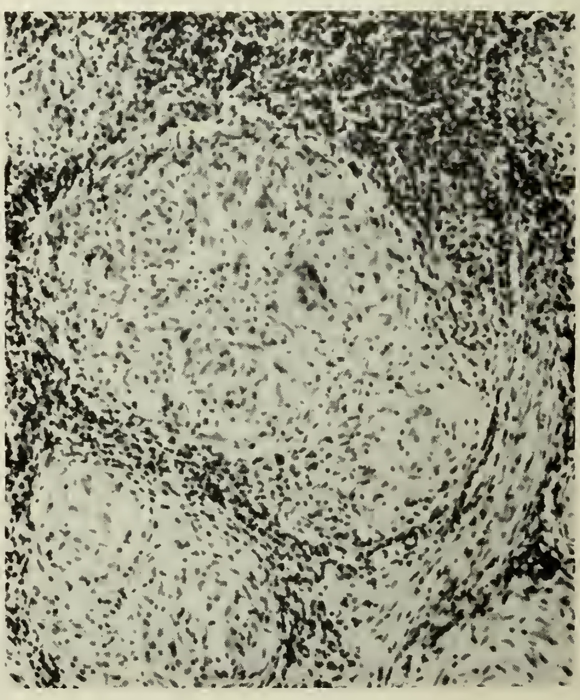

Fig. 1. Lymph node biopsy showing typical noncaseating granuloma with multinucleated cell (H and E × 100)

ERNEST J. CLARK *and* ALSTON W. BLOUNT *are both with the Department of Medicine, USAF Hospital Carswell.*

decreased on the electrocardiogram but was otherwise unchanged. There had been further increase in heart size on the chest X-ray. Carbon dioxide angiocardiography at this time showed a 25 mm. soft density interposed between the gas shadow in the right atrium and the atrial border, presumably representing pericardial fluid.

Coumadin® was discontinued at this time and prednisone in the amount of 60 mg. daily was restarted. He continued to receive digitalis. Over the next few days the pulse pressure gradually narrowed to almost zero and a marked paradoxical pulse appeared. Because of these signs of possible cardiac compression, a pericardiocentesis was unsuccessfully attempted. His condition failed to improve and there was no apparent response to mercurials and digitalis. On Jan. 22 a thoracotomy was performed with the intent of doing a pericardiectomy. At surgery the pericardium was of normal thickness but the pericardial sac contained 200 cc. of serosanguinous fluid. The heart was massively enlarged and the right ventricular wall extremely thin. During the procedure various arrhythmias developed terminating in cardiac arrest. Spontaneous heart beat was finally obtained and a normal sinus rhythm established after several minutes. A pericardial window was constructed and the chest closed. Following surgery his condition remained critical, pulmonary edema developed, and he died on the second postoperative day.

At postmortem examination the heart weighed 650 gm. The entire right ventricular wall was extremely thin measuring 2 mm. at its thickest point (Figure 3). The upper septum was also thin and contained irregular pale nodules. The entire endocardium was thickened and there were scattered white fibrous nodules, 2 to 5 mm., over the surface. The left ventricular wall was 12 to 14 mm. in thickness and there were irregular areas of fibrosis and hemorrhage. The coronary arteries and both atria were normal. Sections through the right ventricular wall showed collagenous tissue with only rare muscle fibers. Elastic and amyloid stains were negative. Sections through the left ventricle disclosed scattered lesions infiltrated with lymphocytes, plasma cells, and multinucleated giant cells containing asteroid bodies (Figure 4). There was increased vascularity in these areas and destruction of muscle fibers. The endocardial surface of the right side of the septum showed organized thrombotic material.

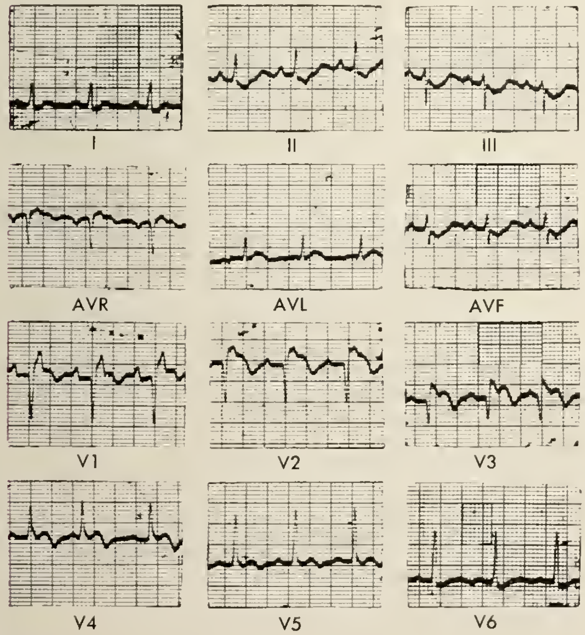

Fig. 2. Electrocardiogram showing changes compatible with anterior myocardial injury

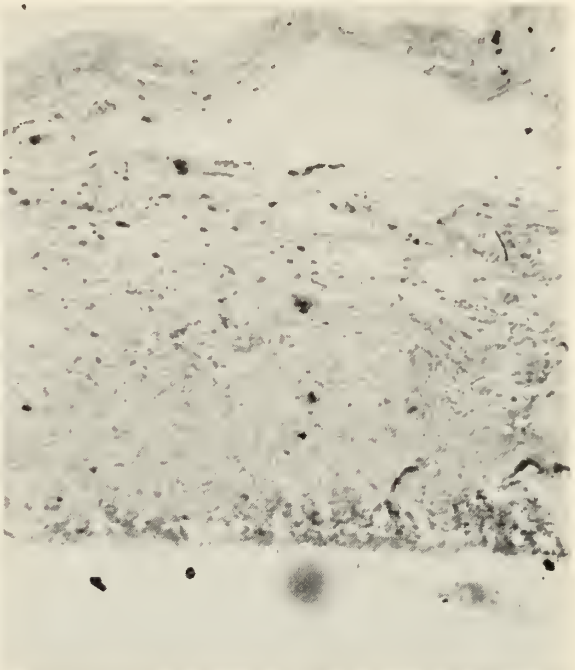

Fig. 3. Section of entire thickness of right ventricular wall. Muscle bundlese are completely replaced by collagenous tissue (H and E × 40)

Examination of sections of the right lung disclosed old infarction with evidence of more recent infarction in the left lung. Hilar nodes were enlarged and on section showed general loss of architecture with giant cells.

DISCUSSION

Fatal myocardial sarcoidosis without pulmonary fibrosis and cor pulmonale is rare. Porter[1] in 1960 reviewed the world literature and collected 33 cases with death directly attributable to myocardial sarcoidosis and added 1 case of his own. He listed another 20 patients with myocardial involvement who died from other causes. Another 7 cases of probable myocardial sarcoidosis without histologic proof were mentioned. In all cases there were other sites of sarcoidosis. Since that time there have been other case reports of fatal myocardial sarcoidosis.[2–5] In reviews of autopsied cases of sarcoidosis the overall incidence of cardiac involvement has been 20%.[6,7]

In the present patient the diagnosis of sarcoidosis was established on the basis of lymph node biopsy with classical granulomatous changes (Figure 1). The development of cardiomegaly and heart failure led to the diagnosis of sarcoid-

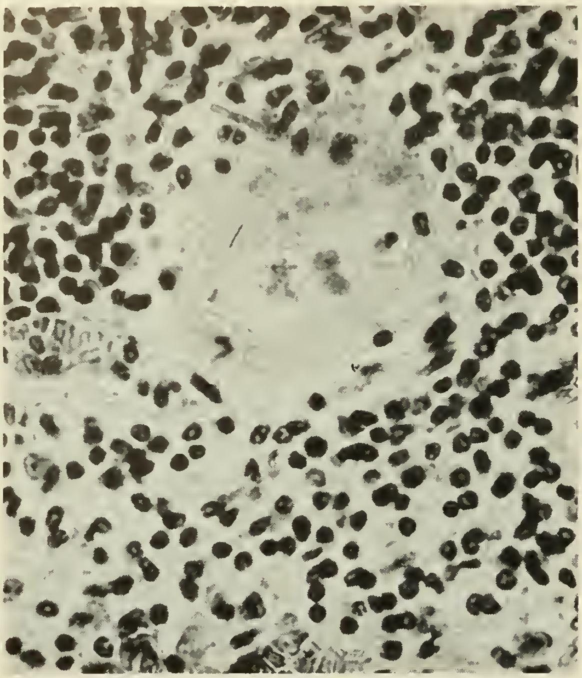

Fig. 4. Section of left ventricle showing a multinucleated giant cell with asteroid body (H and E × 400)

osis of the myocardium. It has been observed that one-third of those with death due to myocardial sarcoidosis had congestive heart failure.[1] The electrocardiographic changes suggestive of acute myocardial injury or infarction were similar to those in other cases.[1,4,8] Digitalis and steroid therapy resulted in improvement in the heart failure temporarily. Gold and Cantor[8] also noted improvement with steroid and digitalis therapy in a patient with similar clinical and electrocardiographic findings. The finding of multiple pulmonary emboli has been lacking in other case reports. Organized thrombotic material on the endocardial surface of the right side of the septum points to the right ventricle as the likely source of emboli.

The clinical picture of pericardial effusion developed with suggestion of impending tamponade. The intravenous carbon dioxide angiocardiography supported this with a 25 mm. atrial band. This value falls within the range of almost certain pericardial effusion according to the studies of Scatliff and associates.[9] The finding of fluid at surgery with a normal pericardium and epicardium would point to heart failure as a likely cause of the effusion. The serosanguinous nature of the fluid may have been related to attempts at pericardiocentesis. Pericardial and epicardial sarcoidosis has been reported in the past,[1,10] but there is no mention of pericardial effusion.

The autopsy finding of marked thinning of the entire right ventricular wall with replacement by collagenous tissue and virtual absence of muscle fibers is an extremely rare finding (Figure 3). There had been no coronary occlusion to account for this. The lack of typical lesions of sarcoidosis in the right ventricle could be explained on the basis that extreme fibrosis without granulomatous changes or giant cells may be the end stage lesion of sarcoidosis.[6] Left ventricular infiltration with lymphocytes and giant cells with asteroid bodies strongly suggested sarcoidosis of the myocardium as the primary disease process. Hines and Sancetta[4] have reported marked thinning and fibrosis of a localized area of the left ventricle in a case of myocardial sarcoidosis simulating a ventricular aneurysm. It would seem that the probable mechanism was infiltration and replacement of the myocardium with sarcoidosis and healing with replacement by fibrosis. Other examples of extreme thinning of the entire right ventricle and atrium,[11] and indeed of the entire heart,[12] differed from the present case in that there was no replacement of myocardium by fibrosis or inflammatory tissue.

SUMMARY

A case of myocardial sarcoidosis with pericardial effusion and marked thinning of the right ventricular wall due to myocardial replacement with fibrous tissue is presented with autopsy findings.

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Cavitating Pulmonary Metastasis Associated with Spontaneous Pneumothorax

M. C. KEW, M.B., B.CH. (RAND) F.C.P. (S.A.)
Johannesburg

Although primary bronchogenic carcinoma frequently undergoes cavitation,[1] this appears to be a rare finding in pulmonary metastases. The first case of cavitation in a pulmonary metastasis was described as long ago as 1871 by Bristowe,[2] but since then only 36 cases have been reported.[1–14]

The association of spontaneous pneumothorax with pulmonary metastases is, likewise, rare. The first case of this sort was reported by De Barrin in 1937[15] and since then 44 cases have been reported in English literature.[12–14, 16–20]

In only 1 case has the sequence of a solid pulmonary metastasis first undergoing cavitation, which was demonstrable radiologically, and then giving rise to a pneumothorax, been described.[12] For this reason, and because our case clearly demonstrates the mechanism of development of the pneumothorax, we report the following case.

CASE REPORT

A 15-year-old girl of mixed Chinese and Portuguese descent fell and struck her right knee when playing at school. Shortly after this she became aware of a painful swelling just above the right knee, and when this grew progressively larger, medical advice was sought. A diagnosis of osteogenic sarcoma of the right femur was made and she was transferred to the Johannesburg General Hospital for treatment. When seen by us for the first time, the local features were those of a sarcoma and X-ray showed a destructive lesion of the lower end of the right femur, the features of which were compatible with an osteogenic sarcoma. This diagnosis was confirmed on biopsy of the tumor. At this stage there was no evidence of dissemination of the tumor and an X-ray of the chest was adjudged perfectly clear. It was decided to treat her with radiation and she was given a total dose of 7,000 rads to the tumor and 6,000 rads to the adjacent femur in the radiotherapy department of the Johannesburg General Hospital (Dr. N. de Moor). She remained reasonably well throughout this period and there was no evidence of dissemination of the tumor. She was sent home with a view to reassessing her after six months. If at this stage there was no evidence of dissemination, the affected limb was to be amputated. She was a little tardy in returning and was seen again nine months later when an X-ray of the chest showed a small, solid, ovoid opacity in the right middle lobe (Fig. 1). A repeat X-ray one month later showed that the once solid tumor had become a thin-walled cavity (Fig. 2). An inflammatory lesion, more particularly tuberculosis, was suspected. But tuberculin testing, sedimentation rate, and examination of sputum and gastric washings for tubercle bacillus were all negative. A further X-ray done one month later showed the development of a pneumothorax on the right side (Fig. 3). This event had been clinically silent and she showed no evidence of respiratory distress. There was still doubt as to whether this was inflammatory or neoplastic in origin. When she returned three months later the lesion had grown considerably and still showed the original cavity at its upper pole (Figs. 4 and 5). The pneumothorax

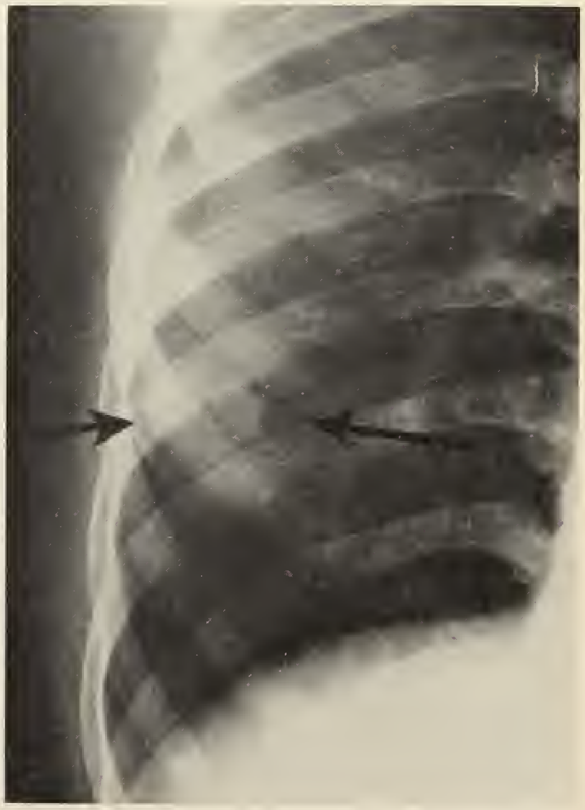

Fig. 1. Chest X-ray showing solid, ovoid metastasis in right middle lobe.

M. C. KEW *is registrar, Johannesburg General Hospital and Department of Medicine, University of the Witwatersrand Medical School, Johannesburg.*

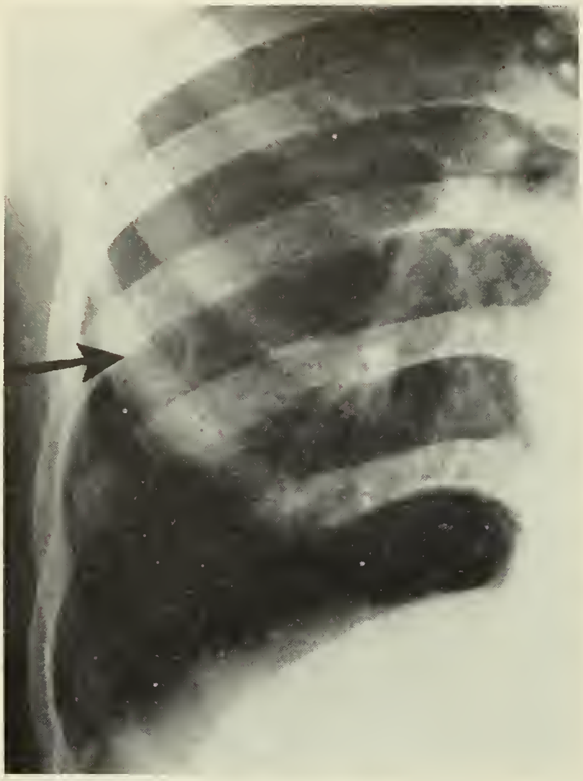

Fig. 2. Repeat X-ray one month later showing once solid tumor now formed a thin-walled cavity

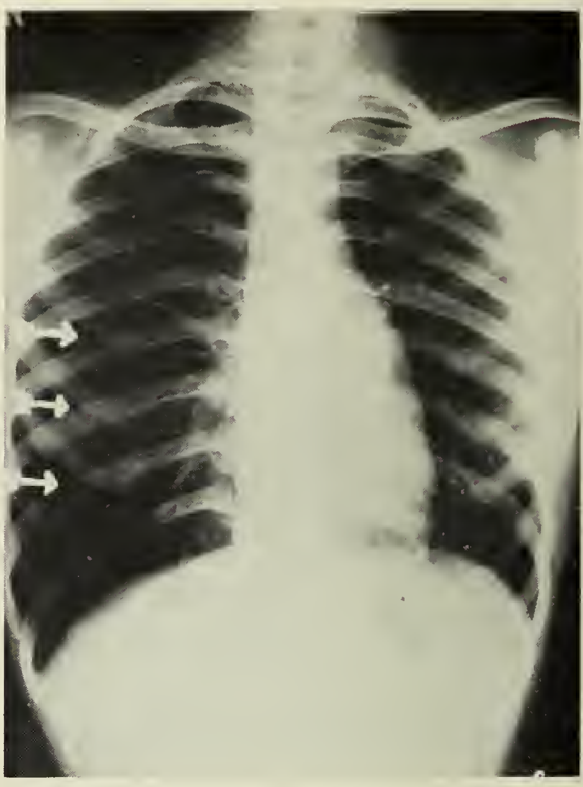

Fig. 3. Repeat X-ray one month later showing development of partial pneumothorax on right

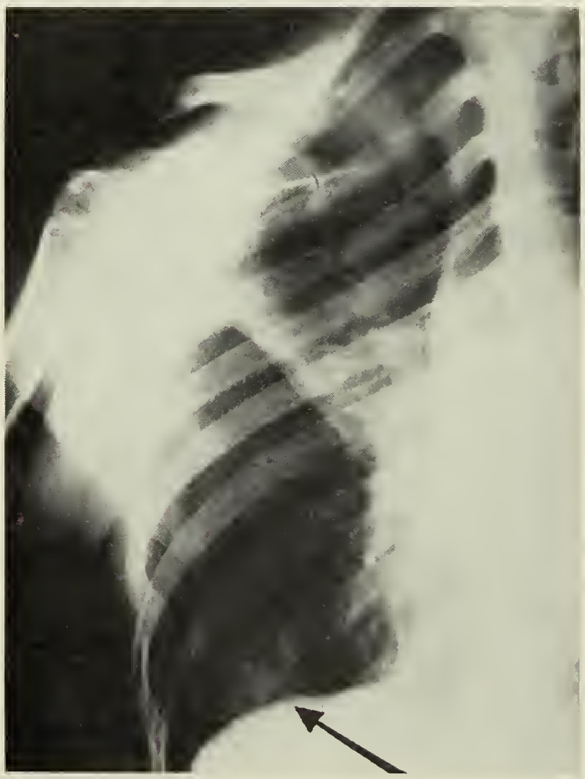

Fig. 4. X-ray taken three months later showing increased size of tumor with original cavity still visible at upper pole. Note pneumothorax is present and unchanged.

was still present and unchanged. In addition, there now was a small, bloodstained effusion at the right base. We felt that she satisfied all the criteria which should be fulfilled before undertaking surgical resection of a pulmonary metastasis. She was in good general condition, she was feeling well, gaining weight, and her hemoglobin was 14.7%. The erythrocyte sedimentation rate was 8 mm. in one hour (Westergren), with normal serum proteins. The primary tumor was under control. There was no evidence of dissemination of the tumor to sites other than the lungs. There was present what we thought was a solitary pulmonary metastasis. A thoracotomy was therefore performed. The pleura was quite normal. There was a single subpleural metastasis in the right middle lobe. It was hemorrhagic in appearance and measured 3 x 2 x 2 cm. (Fig. 6). When the anesthetic bag was pumped, gas escaped from a hole in the tumor (arrowed in Fig. 6). A middle lobectomy was performed. The patient made an uneventful postoperative recovery and follow-up X-ray showed that the right lung had completely reexpanded. Histological section of the tumor confirmed diagnosis of osteogenic sarcoma metastasis.

DISCUSSION

In those cases of pneumothorax associated with pulmonary metastases in which necropsies have been performed, 2 mechanisms accounting for the development of the pneumothorax have been described—firstly, the development of a malignant bronchopleural fistula. This was first described by Thornton and Bigelow[20] as being

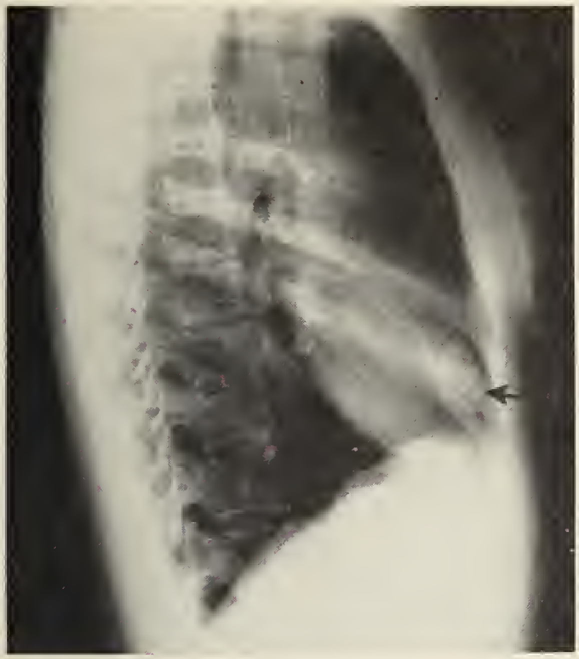

Fig. 5. Lateral view of Fig. 4.

present in one of the 2 cases they reported in 1944.

For the development of a malignant bronchopleural fistula, there are 3 essential prerequisites: First, the tumor, whether primary or secondary, must erode into a bronchus or bronchiole; second, the tumor must undergo necrosis and liquefaction, the contents then being discharged into the bronchus or bronchiole and a cavity resulting. The tumor contents have been recognized in sputum on 1 occasion.[5] Four possible causes of necrosis of pulmonary tumors have been postulated: a rapidly growing tumor may outstrip its blood supply, the central area undergoing ischemic necrosis and liquefaction;[1,12] the tumor may become secondarily infected with abscess formation;[1] necrosis may follow radiation to the tumor;[16] finally, certain metastases secrete a softening material which may result in liquefaction, for example, keratin producing squamous carcinoma of the tongue or mouth.[7] Although necrosis is not infrequently seen in pulmonary metastases at necropsy, unless there is erosion into a bronchus or bronchiole, cavitation does not occur. The infrequency of this occurrence, together with the fact that pulmonary metastases rarely have an inadequate blood supply, have been suggested as causes for the infrequency of cavitation in pulmonary metastases.[12]

The third prerequisite is that the metastasis be subpleurally situated so that erosion through the pleura occurs, giving rise to a malignant bronchopleural fistula.

The sequence of a solid pulmonary metastasis first undergoing cavitation and then giving rise to a pneumothorax was present in 1 of the 2 cases described by Salzman and associates[12] and also in our case. In their case no necropsy was performed so that the mechanism of the formation of the pneumothorax was not clarified. As our case went to thoracotomy, we were able to demonstrate the subpleural metastasis eroding through the pleura, establishing a malignant bronchopleural fistula (Figs. 6 and 7). As this was demonstrated at thoracotomy, it excluded the possibility that the rent through the pleura was an artefact created during necropsy, as suggested by D'Angio and Lannaccone in 1961.[17]

The second possible cause of the pneumothorax associated with pulmonary metastases is by rupture of a subpleural bleb. These blebs arise secondary to interstitial emphysema, the air tracking along interlobular septa to the pleura or the mediastinum, as described by Macklin in 1939.[4] The interstitial emphysema may arise in 1 of 2 ways: first, a cavitated metastasis not in contact with the pleura may erode into the surrounding tissue, allowing the escape of air into the interstitial spaces. Second, the tumor, either solid or cystic, may partially obstruct a bronchus or bronchiole, producing a ball-valve effect[19] with progressively increasing intraalveolar tension, which may eventually rupture, giving rise to interstitial emphysema. Rupture of the alveoli may be facilitated by the tumor invading and obliterating blood vessels, thus reducing the

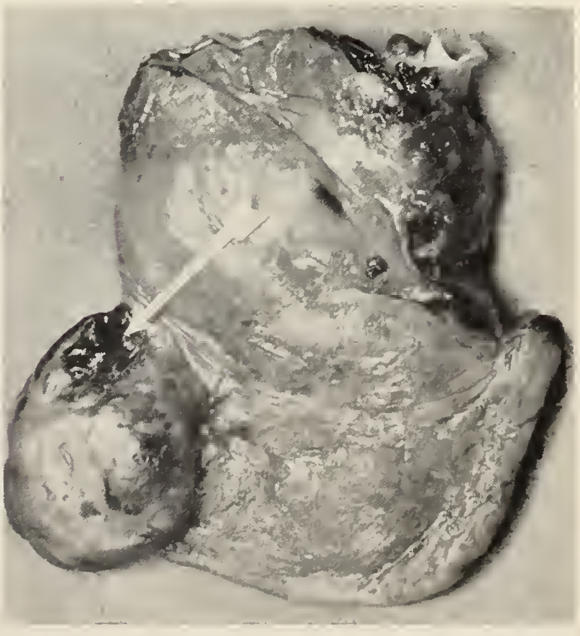

Fig. 6. Naked eye appearance of metastasis with bronchopleural fistula arrowed

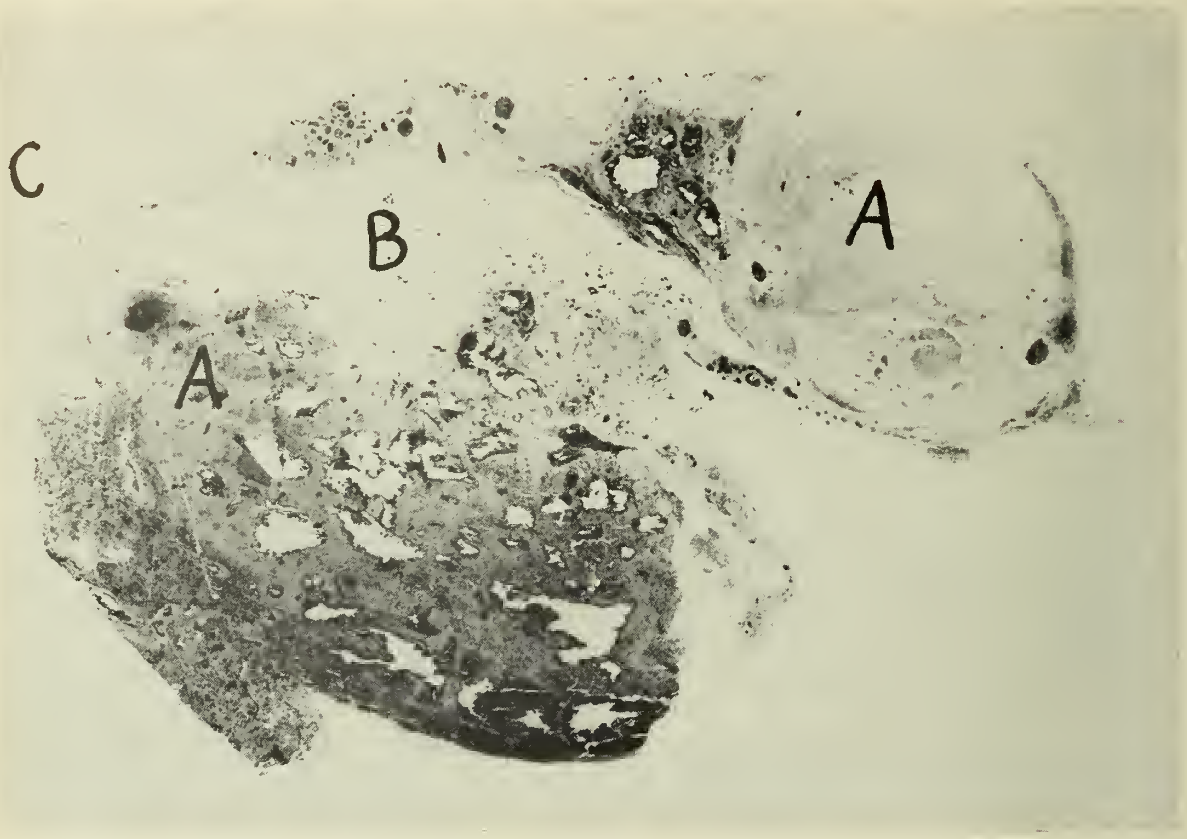

Fig. 7. Section through tumor showing necrotic tumor tissue: (A) with central cavitation (B) erosion through visceral pleura (C) establishing a bronchopleural fistula

tensile strength of the tissues and rendering them liable to tearing and separation.[19]

SUMMARY

A case of osteogenic sarcoma of the femur with a pulmonary metastasis which first cavitated and then eroded through the visceral pleura, giving rise to a pneumothorax, is reported. The possible mechanisms of development of the pneumothorax in these cases is briefly reviewed.

I wish to thank Dr. H. van Wyk, medical superintendent of the Johannesburg General Hospital for permission to publish this case report. I would also like to thank Mr. G. Katz for helpful advice and Mr. S. Shewitz of the photographic unit of the medicine department, University of Witwatersrand for the photographs.

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Heart Disease Secondary to Postnephrectomy Arteriovenous Fistula

JOHN MORGAN, M.D., F.R.C.P.(C)
Calgary, Alberta, Canada

AMONG THE CAUSES of correctable heart disease is the occurrence of a large arteriovenous fistula. This report will describe a case of postnephrectomy arteriovenous fistula. Only three cases of this entity have been reported in the past.[1–3] Peripheral arteriovenous fistulas are usually diagnosed early due to their location, and their small size rarely leads to heart failure. Large, deep-seated, arteriovenous fistulas located close to the aorta or arising from one of its main offshoots are hidden anatomically in the pelvis or retroabdominal area[1–4] and may persist for many years until heart failure develops. Thus, delay in diagnosis, along with the size of the fistula, is the main factor leading to heart failure. A case of postnephrectomy arteriovenous fistula, found fourteen years after nephrectomy, is to be reported. The importance of history and physical examination will be emphasized as this case, along with other deep-seated fistulas,[4] can be diagnosed fairly accurately without special diagnostic procedures.

CASE REPORT

A 46-year-old salesman was referred by Dr. L. A. McKercher on November 26, 1963, complaining of listlessness, ease of fatigue, and breathlessness over six months.

History. There was no history of rheumatic fever. As a young man he had recurrent, sharp, left abdominal pains. In 1941 at the age of 25 years, he joined the RCAF and served as a mechanic, leading an active life without symptoms. After discharge in 1945, he began to have left abdominal pains again and, in 1949, at the age of 32, a left nephrectomy was carried out for hydronephrosis. There was no unusual bleeding problem at surgery. He passed a life insurance examination in 1956 and got along well until the early summer of 1963, when he developed listlessness, ease of fatigue, and shortness of breath. He became quite short of breath if he walked one block or climbed a half flight of stairs. Palpitations developed, and he was aware of his heart action if he exerted himself.

Family history. His mother, age 77, has high blood pressure and his father died at 72 of a cerebral hemorrhage. A 55-year-old sister has hypertension and a 58-year-old brother had bronchial asthma.

Physical examination revealed a flushed, mildly breathless man in his early forties. He did not look chronically ill. His height was 5 ft. 8¼ in. and weight 143¾ lb. Lying back in bed with his head propped on two pillows, a distinct venous pulse was noted with a venous pressure level 4 cm. above the sternal angle. The peripheral arterial pulses were full and the blood pressure was 188/70 in both arms. His heart was enlarged both to the left and right. The apical impulse could be felt in the fifth interspace in the left midaxillary line. The precordial action was increased, and a third heart sound could be heard as well as a grade two, high-pitched, early and midsystolic murmur at the apex. This murmur radiated more faintly to the lower left sternal edge. Normal splitting of the second sound took place in the pulmonary area with inspiration. His liver margin was felt 4 cm. below the costal margin in the right midclavicular line. This organ was tender. The lung fields were clear. In the left subcostal area posteriorly and down over the left flank, a continuous thrill and murmur could be felt and heard. The maximal intensity of this continuous murmur occurred over an old, left nephrectomy scar. The balance of his examination, including rectal examination, was normal.

Chest fluoroscopy and chest films. Considerable general heart enlargement was seen (Fig. 1). Both ventricles were enlarged, and the left atrium extended back to the spine. The cardiothoracic ratio was 18/30 cm. The heart had a full, rocking action with increased pulsations of the aorta and main pulmonary artery.

Electrocardiogram. The broad, negative P wave in V_1 and a diphasic P wave in V_2 suggested left atrial hypertrophy (Fig. 2).

Laboratory. Routine blood studies were normal. His hemoglobin was 15.6 gm. per ml. The hematocrit was 47% and the mean corpuscular hemoglobin concentration 33%. The sedimentation rate was 1 mm. per hour (Westergren). White blood count was 6,100 per cubic milliliter with 53% polymorphonuclear cells, 2% band forms, 5% eosinophils, 34% lymphocytes, and 6% monocytes. Urinalysis was negative, with the urine having a specific gravity of 1.017. The blood urea nitrogen was 20.3 mg. per 100 ml.

A clinical diagnosis of postnephrectomy arteriovenous fistula with early congestive heart failure was made and he was admitted to the Holy Cross Hospital in Calgary on Dec. 1, 1963. After one week's bed rest and salt restriction, the patient's gallop sound became less prominent. An aortogram (Fig. 3A and B) was done using the Seldinger technique[5] in order to avoid a direct puncture in the region of the fistula. A large left arterio-

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JOHN MORGAN *is at Holy Cross Hospital, Calgary, Alberta, Canada.*

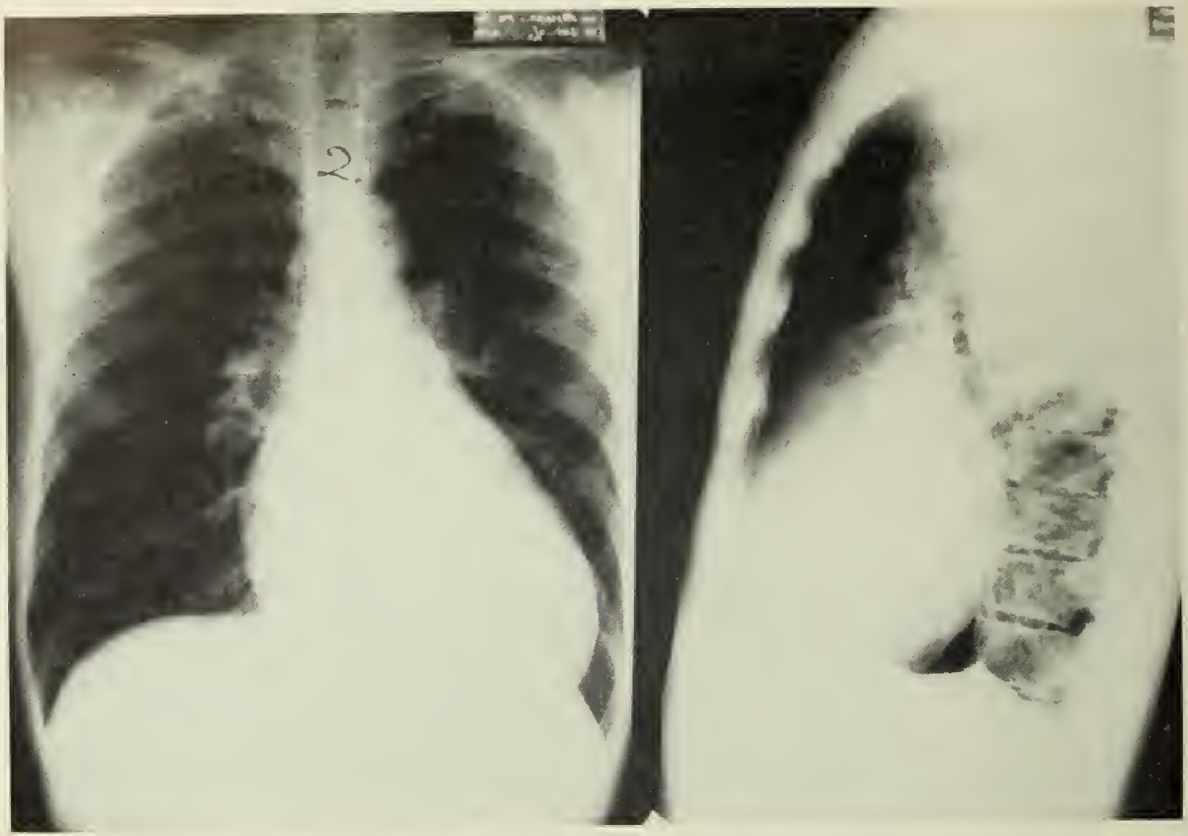
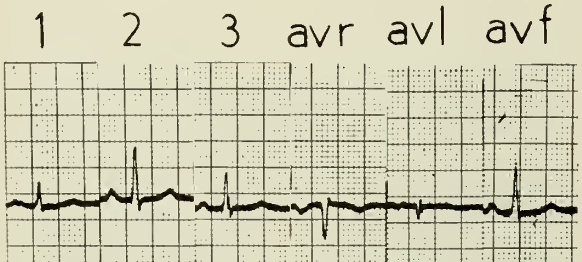


Fig. 1. Preoperative chest films. Posteroanterior and left lateral views. The cardiothoracic ratio is 18/30 cm.

venous fistula in the renal bed was confirmed and the films showed striking dilatation of the inferior vena cava above the fistula. On Dec. 11, 1963, the arteriovenous fistula was closed and excised by Dr. George Miller.

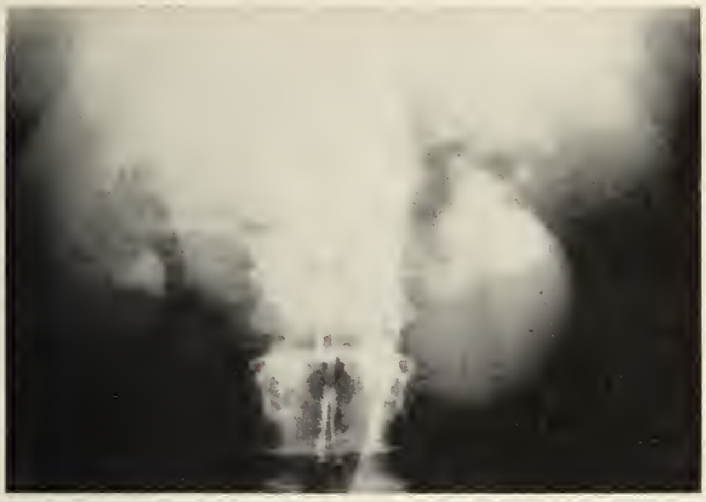
Operative procedure. An anterior incision extending from costal margin to costal margin was made, and an exposure of a 4 × 8-cm. arteriovenous fistula was made. Large satellite veins also drained into the fistula. The fistula was excised and the stumps of the left renal artery and vein were ligated. The thrill was obliterated. The resected specimen showed scattered eggshell calcifications in its wall.



No problems occurred in the postoperative period. His blood pressure ranged from 138/88 to 154/88 in the remaining ten days in hospital, and on the eighth day, chest films (Fig. 4) showed a reduction in the cardiothoracic ratio from 18/30 to 15.5/30. The patient had complete relief of his symptoms and returned to work four weeks after the operation.

Course since operation. He was evaluated three months after operation, at which time his blood pressure ranged from 152/92 to 178/105 mm. Hg. Clinically, his heart size was normal and the apical systolic murmur and gallop sound were no longer heard. The electrocardiogram showed a clearing of the signs of left atrial overloading (Fig. 5). Six months after the fistula was removed, his blood pressure ranged from 198/98 to 186/110 mm. Hg, and he had no symptoms. His chest films (Fig. 6) showed a further reduction in his heart size, with a cardiothoracic ratio of 12.5/30. Reserpine and chlorothiazide therapy was begun, and twelve months after removal of the fistula, he was normotensive and symptom free.

Fig. 2. Preoperative electrocardiogram. Note the deep, negative P wave in V_1 and diphasic P wave in V_2. There are deep S waves in the early precordial leads (standardized 1 cm. = 1 mv.).



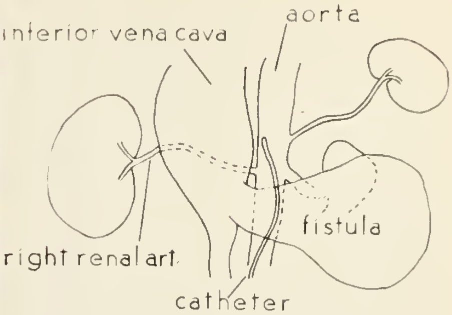


Fig. 3. [A] Aortogram demonstrating a left postnephrectomy arteriovenous fistula. Note the marked enlargement of the inferior vena cava after it drains the arteriovenous fistula. [B] Diagram showing orientation to Figure 3A

DISCUSSION

If a high-output state, with an active, enlarged heart is found, a careful history inquiring particularly as to previous trauma or surgery is important. Examination, including auscultation of flank or abdominal scars[3,5] may reveal the continuous murmur of an arteriovenous fistula. Rectal or pelvic examination may reveal a pulsating arteriovenous fistula.[4]

The heart failure is high-output in type. Chest fluoroscopy is helpful, revealing an active heart with enlargement of the ventricles and increased pulsations of the aorta and pulmonary artery.

Similar cardiac findings occur in other high-output states such as hyperthyroidism, severe anemia, varieties of congenital heart disease with central shunting, Paget's disease, and beriberi heart disease. The feature that distinguishes arteriovenous fistula is the finding of a continuous murmur with systolic accentuation at the site of the fistula.[7]

With the runoff of an arteriovenous fistula,

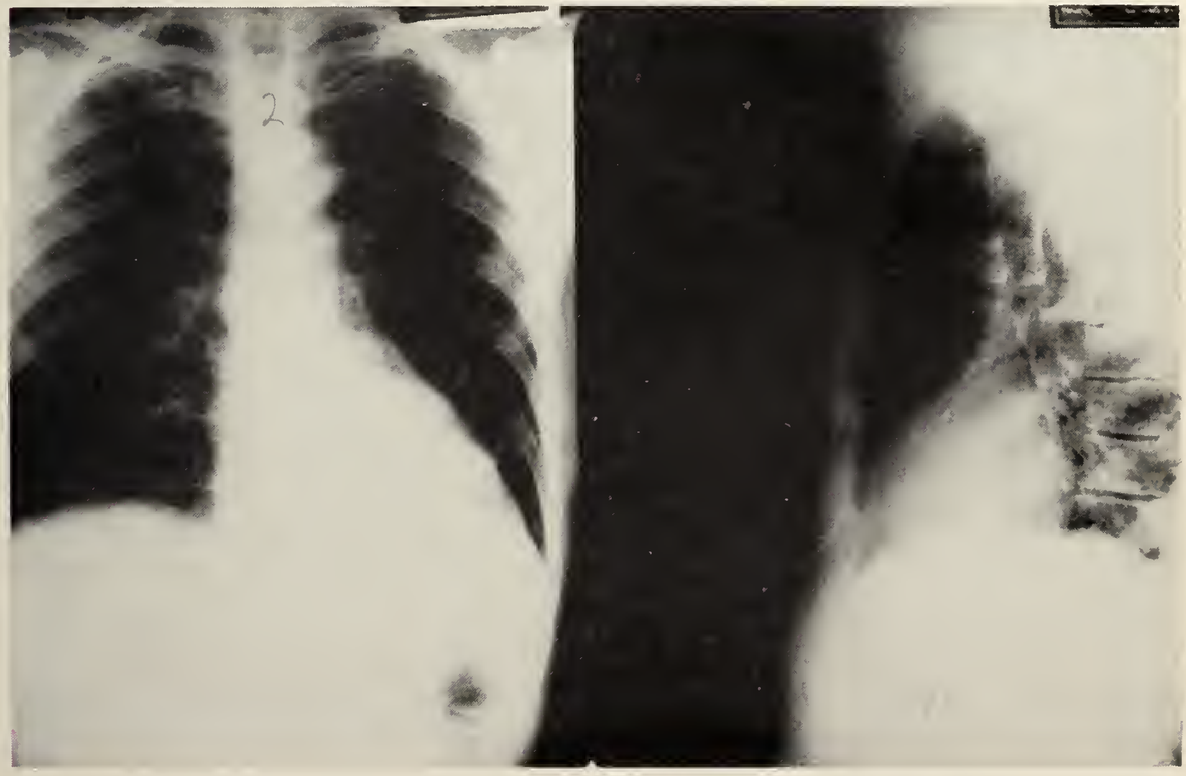


Fig. 4. Chest films, posteroanterior and left lateral, eight days after removal of the arteriovenous fistula. The cardiothoracic ratio is 15.5/30 cm.

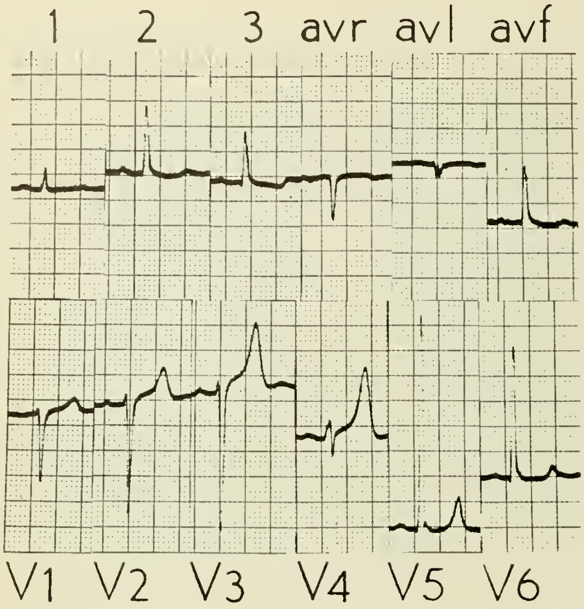


Fig. 5. Electrocardiogram (three months postoperative). The P waves in V_1 and V_2 have returned to normal (standardized 1 cm. = 1 mv.).

the pulse pressure widens, the diastolic pressure falls, and the stroke output is increased. With excision of the fistula, previously masked hypertension may appear.

The delay between nephrectomy and the diagnosis of postnephrectomy arteriovenous fistula in the four cases reported in the literature, including the present case—five years (1), fourteen years, seventeen years (3), and twenty-nine years (2)—suggests that there is little general appreciation of this condition.

SUMMARY

A case of postnephrectomy arteriovenous fistula is reported. Although the condition is rare, there being only three previously reported cases in the English literature, it represents a curable form of heart disease.

Hypertension was masked by the runoff effect of the fistula, and following removal of the fistula, hypertension appeared. Postnephrectomy arteriovenous fistula is a different entity from renal arteriovenous fistula. The postnephrectomy arteriovenous fistula is similar in pathophysiology to other large arteriovenous fistulas that occur close to or from the aorta.

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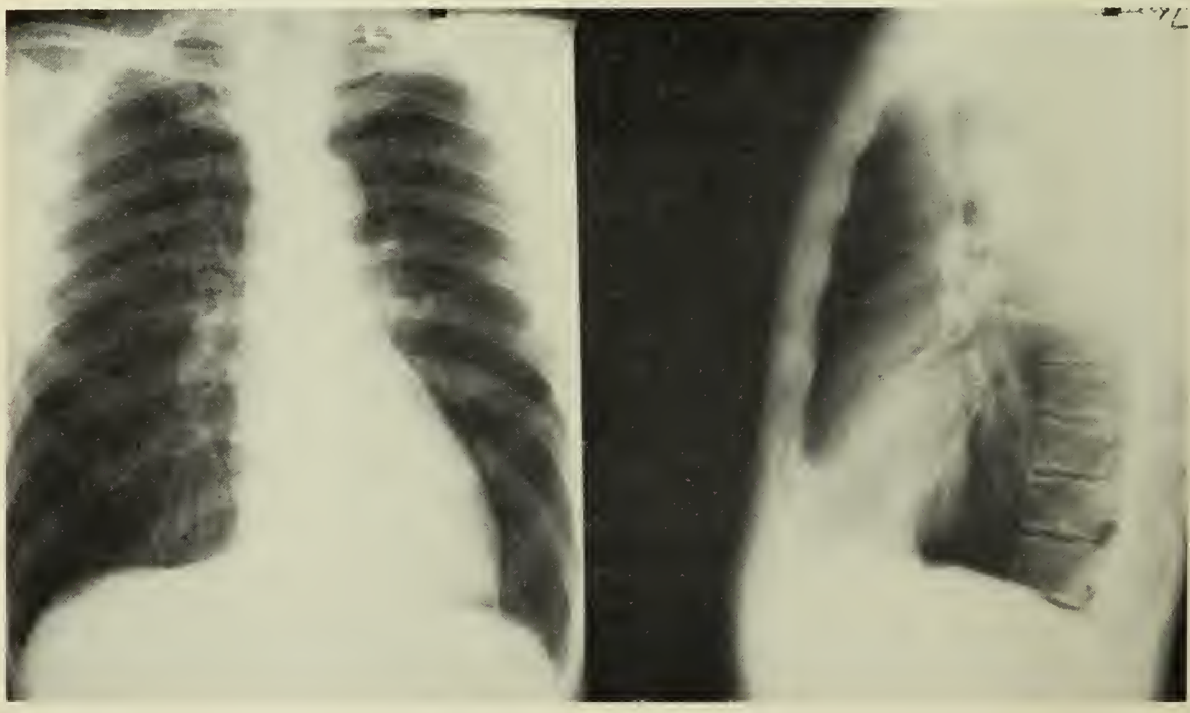

Fig. 6. Chest films, posteroanterior and left lateral, six months after removal of the arteriovenous fistula. The cardiothoracic ratio is 12.5/30 cm.

Thoracic Duct Cyst of the Mediastinum

A Case Report

MALCOLM J. THOMAS, M.D., PAUL W. SANGER, M.D.,
FREDERICK H. TAYLOR, M.D., and FRANCIS ROBICSEK, M.D.
Houston, Texas, and Charlotte, North Carolina

Although the occurrence of lymphatic cysts of the neck and other areas is not unusual, a review of the literature has indicated that primary cysts of the thoracic duct are rare. The first reported case of a supradiaphragmatic thoracic duct cyst was found accidently during an autopsy examination; it was described by Carbone[1] in 1892. Three other cases of supradiaphragmatic cysts found at postmortem examination have been reported since that time.[2]

Two cases of thoracic duct cysts which were diagnosed during life have been reported in American literature. In 1950 Emerson[2] reported the case of a 20-year-old female in whom a right posterior mediastinal mass was detected on a routine chest X-ray examination. At operation, a chyle-filled cyst arising from the thoracic duct was found. In 1954 Bakst[3] reported the second case of thoracic duct cyst in a 42-year-old male. A routine chest film showed a right posterior mediastinal mass lying just above the diaphragm. Upon opening the chest, a chyle-filled cyst was found; the cyst arose from the thoracic duct, which entered the mass inferiorly and ended in a blind pouch superiorly. A third patient with a thoracic duct cyst was recently operated upon by the authors.

CASE REPORT

A 43-year-old asymptomatic male was admitted to Charlotte Memorial Hospital on Aug. 5, 1962. A routine preemployment chest X-ray film had demonstrated a mediastinal mass. On admission the patient appeared to be a healthy, 219 lb. male with no physical abnormalities. Routine laboratory examinations showed the contents of his blood and urine to be within normal limits. The patient's serology report was negative. A posteroanterior chest film (Fig. 1) demonstrated a double shadow over the aortic knob in the left chest. Laminagrams (Fig. 2) of the mediatinum showed a round, 4 cm. mass at the level of the aortic arch. The density of the mass could not be distinguished from the aortic shadow. No involvement of the trachea, left main-stem bronchus, or pulmonary artery was noted. Angiograms showed no communications between the mass and the aortic arch. The preoperative clinical impression was suggestive of a posterior mediastinal cyst or neurogenic tumor.

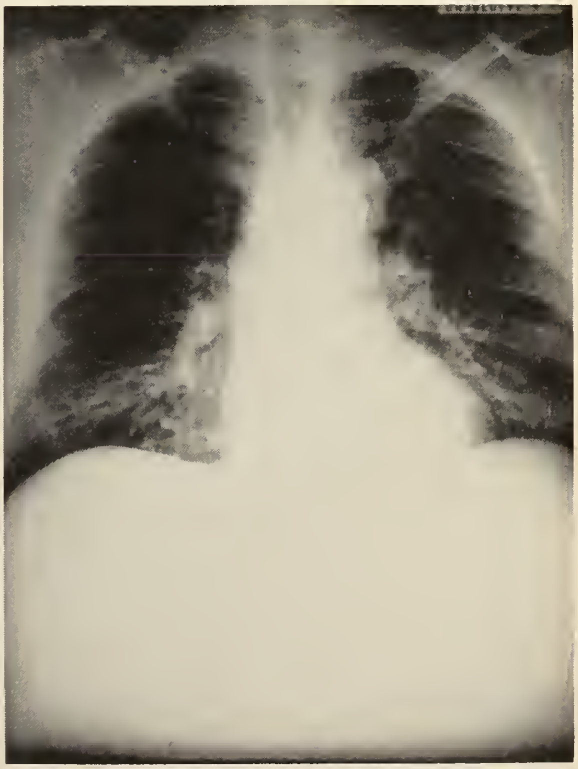

Fig. 1. Posteroanterior X-ray of chest. Round shadow of cyst is visible behind aortic arch.

MALCOLM J. THOMAS *is with the Department of Surgery, The University of Texas M. D. Anderson Hospital and Tumor Institute, Texas Medical Center, Houston.* PAUL W. SANGER, FREDERICK H. TAYLOR *and* FRANCIS ROBICSEK *are with the Heineman Foundation Laboratories, Charlotte Memorial Hospital, Charlotte.*

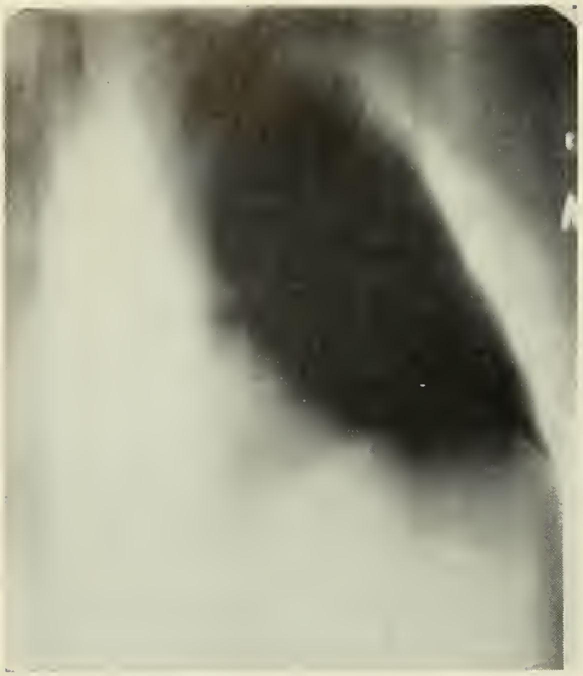

Fig. 2. A laminagram shows mass in posterior mediastinum.

On Aug. 6, 1962, the chest cavity was entered through a left posterolateral thoracotomy incision. A cystic structure was found in the posterior mediastinum, superior to the aortic arch and medial to the left subclavian artery. The overlying pleura was incised and a cyst containing milky fluid with particles of fat swirling about in it was visualized. The lesion was easily enucleated. At the base of the cyst a small pedicle, which arose from the thoracic duct, was ligated and divided. The mediastinal pleura was approximated, and the chest was closed. The patient's postoperative course was uneventful and he was discharged on the eighth postoperative day.

Gross examination showed the specimen to be a grayish-tan, thin-walled, ovoid, cystic structure measuring 7 × 6 × 2.5 cm. Portions of a bright yellow connective tissue were attached to the outer surface. The wall of the cyst varied from 1 to 2 mm. in thickness. The inner surface was finely trabeculated. Microscopic examination verified its identification as a thoracic duct cyst.

SUMMARY

A thoracic duct cyst was successfully excised from a 42-year-old man. This is only the third such cyst to be found during life that has been reported in literature. The cyst originated in the thoracic duct superior to the thoracic aortic arch and medial to the left subclavian artery.

None of the 3 reported cases demonstrated characteristics which could lead to an exact preoperatively diagnosis. All 3 cases showed a posterior mediastinal mass on routine chest X-ray films. The removal of these cysts is warranted since an exact diagnosis can be established in no other way.

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Book Reviews . . .

Heritable Disorders of Connective Tissue

by VICTOR A. MC KUSICK, *499 pp., ill., C. V. Mosby Co., St. Louis, 1966. $18.50*

This third edition of Dr. McKusick's book is an excellent summary of current concepts involved in the accumulated knowledge concerning the so-called genetically determined disorders of connective tissue. There are some new sections embracing relatively up-to-date ideas of protein synthesis and the molecular basis for various genetic aberrations. In the first chapter the author states that "discussion of the genetics of common connective tissue disorders, such as systemic lupus erythematosus, is beyond the scope of this book." Despite the more than fashionable L. E. test, lupus is not a "common connective tissue disorder." Since the familial aggregation of lupus and rheumatoid arthritis has been seriously challenged by the studies of O'Brien and Bunim, it seems wise to leave these two disorders out of the discussion.

The chapters dealing with the specific entities which interest Dr. McKusick—particularly the Marfan syndrome—are well organized and illustrated. In some instances a profusion of clinical examples obscures the lack of basic knowledge into the biochemical defects in these disorders, but this is really no criticism of the author's approach—only an evaluation of our pose or inclination at this stage of knowledge.

This book is a superlative clinical commentary on those disorders of connective tissue which are now considered to be on a hereditary basis. One only ponders, perhaps prematurely, the lack of basic knowledge related to the mechanisms involved in those disorders.

RALPH C. WILLIAMS, JR., M.D.
Minneapolis

Two Noncardiac Cases of Disease, with Cardiological Implications

GEOFFREY BOURNE, M.D., F.R.C.P., F.C.C.P.

London

CERTAIN MEDICAL THEORIES have a general application which is not confined to one branch of the science. Described here are 2 examples. They are not cardiological, but illustrate principles which have considerable importance to cardiologists.

CASE REPORTS

Case 1. Twenty-three years ago the writer, then cardiologist to St. Bartholomew's Hospital, met with an unusual and educative case. This was one of the occasional general medical problems met with among the large majority of cardiological ones—for in those days the teaching of internal medicine was part of the daily duty.

The patient was an Armenian, a man of 42, who had been called up for military service. After some months of training as a private soldier in the infantry, he began to complain of rather vague sensations in the legs and feet. These were accompanied by lassitude and unspecified feelings of general ill-health which were ignored by the authorities.

In an attempt to escape from the drudgery and fatigue of infantry life, the man applied for and obtained permission to study Japanese with a view to a post in the intelligence department. He was a highly gifted and hypersensitive person and his racial facility for languages aided his considerable progress. His symptoms continued throughout this period, remaining however somewhat vague in character.

One day he fainted on parade and, in the absence of a clinical diagnosis and in lieu of a better solution, he was transferred to a psychiatric hospital. He failed to respond to treatment, was labeled a psychopath, and discharged from the service.

A month or two later, when he was back in civilian life, the writer was asked to see him in consultation with his own doctor. The above history was obtained. In addition, the patient was questioned further and was found to be free from cough, dyspnea, paraesthesia or discomfort in any other area, dyspepsia, diarrhea or constipation, sphincter disturbance, and other symptoms. The only firm complaint was the feeling of abnormality in the legs and feet. This was perfectly symmetrical. Exercise had little effect upon it. The hands were not affected.

On examination the general appearance was normal, the heart was clinically normal, and the blood pressure was about 110/80. The lungs were free from abnormality, the abdominal organs were perfect, the liver being just palpable, and the spleen was not felt. An electrocardiogram was within normal limits. Finally, attention was focused upon the central nervous system. There was no wasting, diminution of movement, or spasticity. The superficial reflexes were normal. The deep reflexes, including the ankle jerks, were present. No loss of sensation, superficial or deep, or by tuning-fork, was detected.

The examiner's attention was fixed upon the following points: The patient appeared to be a perfectly well-adjusted and normal individual. He was a hypersensitive and acute specimen of his race. His description of the abnormal feeling in his feet and legs was quite convincing and suggested an organic cause. There was no multiplicity of symptoms.

Peripheral neuritis of some type or subacute combined degeneration of the spinal cord were suggested and a complete blood count was done. It revealed a slight diminution in the total red blood cell count. The figure was about 3.8 million. The hemoglobin percentage was 82, giving a color index of above 1.1. The white cell count was around 4,000. The picture was typically one of macrocytic anemia, the degree of this being insufficient ordinarily to provoke symptoms but enough, when the patient was under stress, to have caused his attack of faintness.

He was immediately given large doses of B_{12} and slowly improved. After a period of months he had lost all his symptoms. They had not recurred some years later when the writer was called in to see a member of the same family who had heart disease. This elderly uncle of the subacute combined patient had retained his health with the aid of B_{12} injections given at gradually lengthening intervals.

The case has never been forgotten, for it underlined the falsity of the psychiatric diagnosis so easily made, and the dependability, in a really intelligent patient, of obtaining a correct history of an anatomical change before any such lesion was detectable by ordinary clinical means.

Case 2. This patient exemplifies a diagnostic point at the opposite extreme. He was a retired colonel in the 17th Lancers, nearly 69 years of age, and had not been ill in the past except for dysentery forty-five years before, and transient malaria. He suffered from epigastric pain. This had gradually been increasing for nearly a year, at first across the back, but more recently through to the front. It was central in position and increased slightly after gardening or salmon fishing. Over the previous three months it had worsened, becoming constant. It was not increased or diminished by food. It was partially

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GEOFFREY BOURNE *is consulting cardiologist to St. Bartholomew's Hospital, London.*

alleviated by paracetamol (Panadol®). Waterbrash was absent. He had lost 14 lb. but had dieted, having previously been too fat.

On physical examination he looked sallow, but was not anemic. The heart and lungs were normal clinically, the blood pressure was 134/94. No abdominal swelling or abnormality was detected. The pain, in its nature and mode of onset, suggested a carcinoma of the body of the pancreas, as described by the writer in *Lancet*, Dec. 5, 1936, "Pain as the only sign of pancreatic carcinoma."

The patient was admitted to hospital and the following investigations were made:

Red blood count, 4,930,000 per c. mm. Hemoglobin, 100% or 14.8 gm. per 100 cc. White blood cells, 4,800. Differential white count was normal. No abnormalities of red cells were noted. Blood sedimentation rate, 5 mm. in 1 hr. (Westergren). Blood Wassermann reaction, negative. Serum amylase, 129 (Somorgi units per 100 cc.). Blood sugar (fasting), 139 mg. per 100 cc. Urine examination, a faint trace of protein with no other abnormality. No abnormal cytology in centrifugal deposit. Stool examination, wet film of a first stool showed no suggestion of pancreatic deficiency, no excess of fat, and any muscle fibers present appeared to be well digested. Occult blood negative in 2 specimens.

A radiological examination was made during which the attention of the radiologist was particularly directed to the question of pancreatic disease or swelling. A barium meal revealed a normal stomach and duodenum and showed no evidence of pressure upon the stomach from behind by a pancreatic tumor.

In spite of the negative pathological and clinical examinations, and also since the symptom was an isolated one, Mr. Rodney Smith, an expert in pancreatic surgery, was asked to see the patient. He did so and agreed to explore the abdomen, and a pancreatic carcinoma was found. The growth was fixed posteriorly and was inoperable. The exact type of tumor was never known since, owing to the risk of a pancreatic fistula, a biopsy was inadvisable. The patient died a month later.

In this case also the diagnosis was made upon the basis of the history alone. Special investigations, although directed by a clear suspicion of the presence of the growth, were all entirely negative. The lesion, in spite of its size and advanced degree, was undetectable by physical examination or by radiological or pathological tests.

Both these cases have their counterpart in the diagnosis of coronary disease, where a sensible patient complains of typical central chest tightness only when walking fast, or uphill, or in cold weather, or after food, and when it radiates to an arm and is perhaps accompanied by slight dyspnea. True angina of effort is present in such a case even when there is a clinically normal cardiovascular system, a normal 12-lead electrocardiogram, and a normal radiological cardiac picture. The sensory nervous system of an intelligent and sensitive man or woman is in more intimate association with his or her brain than any external instrument can be. If the messages sent by it are correctly described by the patient, and accurately recorded by the examiner, the information will be reliable. The medical history should always be taken, or critically amplified, by the physician in person. It is indeed the most important part of the clinical examination.

BOOK REVIEWS

Heart Disease in Children: Diagnosis and Treatment

by BENJAMIN M. GASUL, M.D., RENE A. ARCILLA, M.D., *and* MAURICE LEV, M.D., *1363 pp., ill., J. B. Lippincott Co., Philadelphia, 1966. $33*

This is a comprehensive reference book of pediatric cardiology, with excellent coverage of the entire field of heart disease in children. The first part of the book is devoted to anatomy, embryology, pathogenesis, pathology, normal prenatal and postnatal circulation, history-taking, physical findings, roentgenology and fluoroscopy, electrocardiography and vectorcardiography, arrhythmias, and cardiac catheterization and angiocardiography.

The various congenital abnormalities are dealt with in a logical and complete manner, and the same format is used for each of the different defects: pathology, hemodynamic, clinical, and roentgenographic features; electrocardiography and vectorcardiography; cardiac catheterization and angiocardiography; diagnosis; prognosis; and treatment. The authors provide numerous references and bibliographies follow each type of congenital defect mentioned as well as each chapter. The general quality of the book is good. The illustrations are well reproduced and adequately described.

This book definitely should be included in the library of any physician or student who has an interest in heart disease in children.

The authors' views are expressed throughout. However, since the section on transposition of the great vessels deals with a controversial type of classification, it would have been helpful if other viewpoints had been quoted. Dr. Lev's thoughts are clearly stated and reflect his writings. Others disagree with his classification and method of approaching transposition of the great vessels; this should have been mentioned in a textbook. A description of the extensive diagnostic use of angiocardiography reflects the views of Dr. Gasul. The angiocardiograms are well illustrated and captioned. However, because several of the congenital cardiac lesions involved are readily diagnosed without angiocardiography, the unwary reader might feel that all types of congenital heart disease need angiocardiography for completeness of diagnosis. In children with ventricular septal defects, the "Eisenmenger" type of hemodynamics may develop, although it is implied in this text that the "syndrome" does not occur until the second decade of life.

In spite of the minor objections mentioned, this is an excellent text which provides a new standard for reference books devoted to heart disease in children. It is highly recommended.

JAMES W. DU SHANE, M.D.
Rochester, Minnesota

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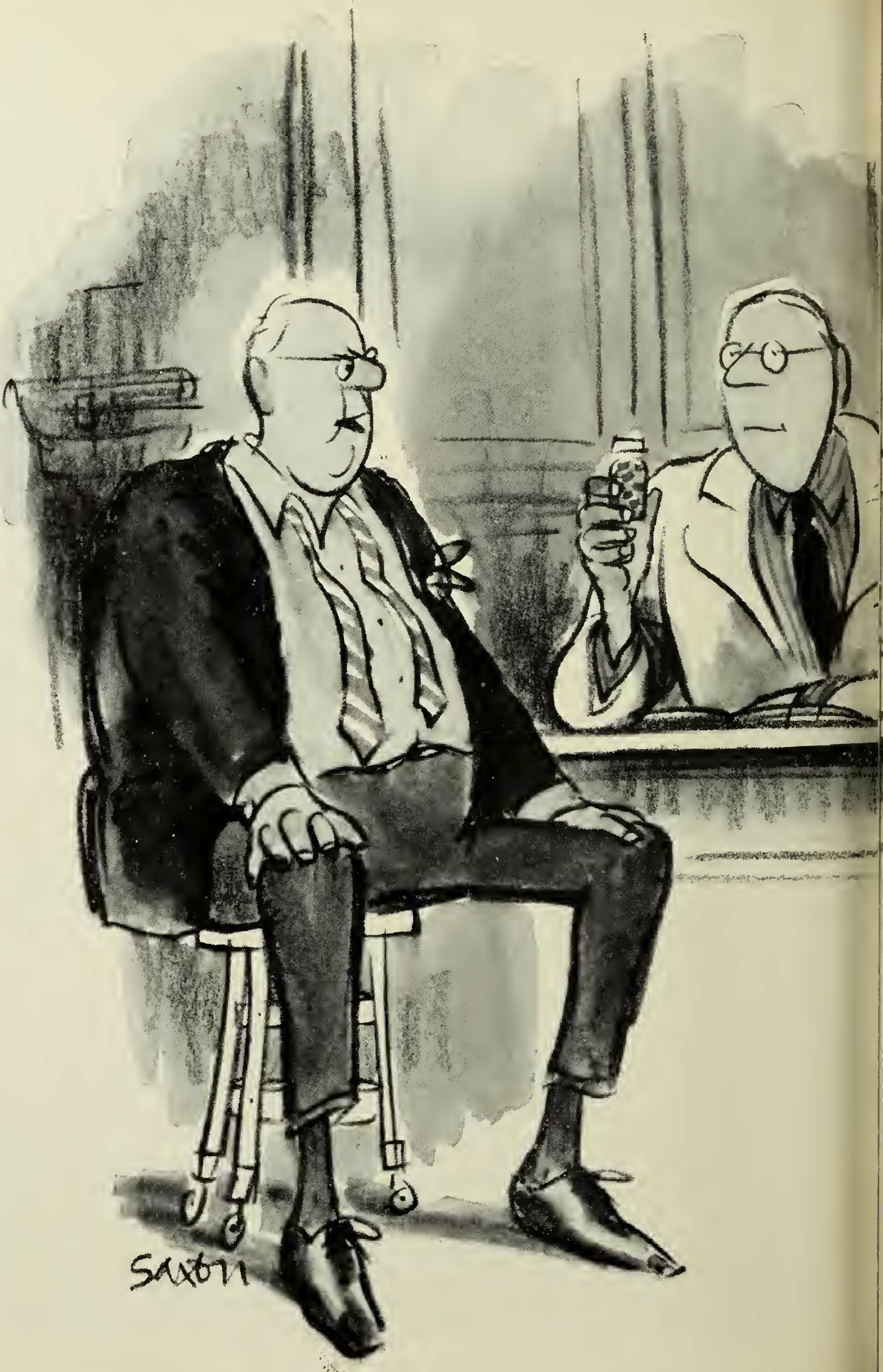
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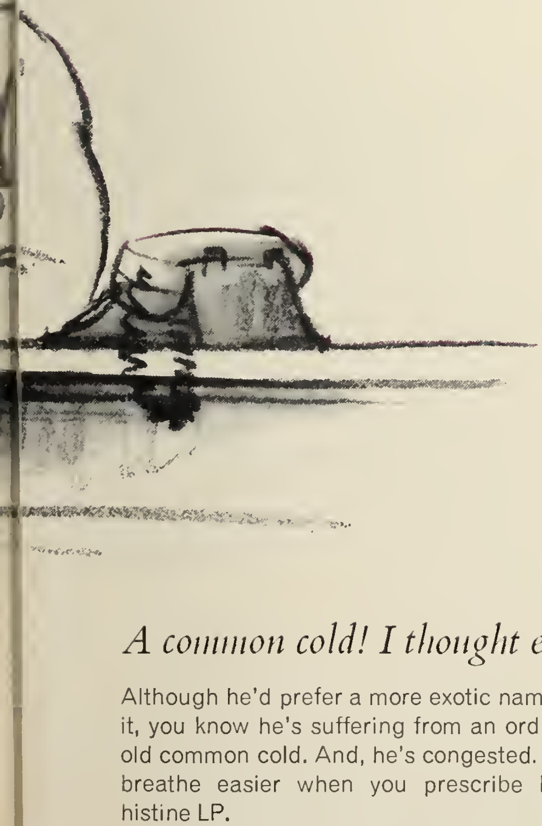

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Book Reviews . . .

The Lung Circulation, Vol. I and Vol. II

by DOMINGO M. AVIADO, *1405 pp., ill., Pergamon Press, New York, 1965. $50 per set*

In the words of C. F. Schmidt whose enlightening introduction begins these 2 volumes, this is a monumental effort. These volumes comprise a complete review of what is known about the pulmonary circulation, to which knowledge the author's extensive researches have made a significant contribution. Volume I is subdivided into a section on the physiology of the pulmonary and bronchial circulation and one on autonomic pharmacology of the pulmonary circulation. Volume II contains sections on cardiovascular and bronchopulmonary drugs, acute cardiopulmonary diseases, and chronic pulmonary hypertension.

One of the outstanding characteristics of this work is the extensive bibliography (there are 6,968 references) for which workers in the field of the pulmonary circulation will be grateful for years to come. Also noteworthy is the generous use of illustrations and tables which serve to amplify the text. On any given subject, all views, including those conflicting with the current consensus, are presented and here perhaps one might have desired greater guidance among the conflicting data by the author whose great experience better qualifies him to make such judgments.

In most of the text the author relies heavily, too heavily perhaps, on the results of his own experiments. Thus, these volumes are an excellent source of the results of the author's numerous investigations when perhaps it might have been preferable to detail some of the ingenious experiments involving the pulmonary circulation by other workers in this field. This would give the reader the opportunity to evaluate the significance of the experimental results presented in the text, in a preliminary way, at least, without the need to consult the original sources.

The format and binding are excellent and most of the figures are well reproduced. Fortunately, an excellent index is included making easy access to the wealth of material included. The cost of $50 for the volumes militates against their purchase by all but the most serious students of the pulmonary circulation. These volumes should be included in all libraries desiring to give a comprehensive coverage of this field.

IRWIN J. FOX, M.D.
Minneapolis

Respiratory Care

by H. H. BENDIXEN, L. D. EGBERT, J. HEDLEY-WHYTE, M. B. LAVER, *and* H. PONTOPPIDAN, *252 pp., ill., C. V. Mosby Co., St. Louis, 1965. $15*

The experience, primarily in the respiratory unit at the Massachusetts General Hospital, is the basis for this book. The first one-third of the book is devoted to physiological principles of respiration. The second one-third considers the practical management of patients requiring respiratory care. The last one-third deals with special problems—chest injuries, myasthenia gravis, neurological problems, and acute exacerbation of obstructive pulmonary disease—that present many respiratory therapeutic difficulties. Unfamiliarity with the nomenclature of pulmonary physiology will necessitate slow reading of the first one-third of the text and delay comprehension of the many fine tables and figures, a factor that cannot be obviated when presenting this subject matter. The main deficiency in the text is the absence of better descriptions of the different types of respirators and their uses, advantages, and disadvantages. In summary, this book is well written, the material is presented in a straightforward manner, and any physician could find much information in its pages that would be of practical value in his everyday practice of medicine.

HAROLD W. EVANS, M.D.
Grand Forks

The Ciba Collection of Medical Illustrations, Vol. 4: Endocrine System and Selected Metabolic Diseases

prepared by FRANK H. NETTER, M.D., *edited by* PETER H. FORSHAM, M.D., *287 pp., ill., commissioned and published by Ciba, Summit, N.J., 1965. $22*

This important fourth volume from the Ciba Collection of Medical Illustrations is of value for its clarification of the complexities of metabolic schemes and their relation to other systems of the body.

The book represents a most difficult challenge to Dr. Netter and his associates in that they are asked to portray graphically what has heretofore been said essentially in words. The paintings are for the most part more diagrammatic, due to the nature of the material, than one would associate with Dr. Netter. However, they are bold, clear, and impressive. The text is a well-done supplement to the art.

The atlas accomplishes its purpose and reflects the time and knowledge that were spent in producing it.

ELTON HOFF
Minneapolis

A Primer of Peripheral Vascular Diseases

by TRAVIS WINSOR, M.D., *and* CHESTER HYMAN, PH.D., *348 pp., ill., Lea & Febiger, Philadelphia, 1965. $12.50*

This compact book fills a real need for clinicians by providing a very concise review of current concepts of peripheral vascular diseases. The introductory chapters dealing with the hemodynamics of blood flow are particularly helpful in providing a brief review of basic physiological concepts of the circulation. The chapters dealing with overall therapy, including surgical procedures, are concise and to the point. The chapter dealing with the history and physical examination of patients with peripheral vascular disease was too abbreviated in the reviewer's opinion. The individual chapters dealing with specific peripheral vascular problems are excellent.

(Continued on page 20A)

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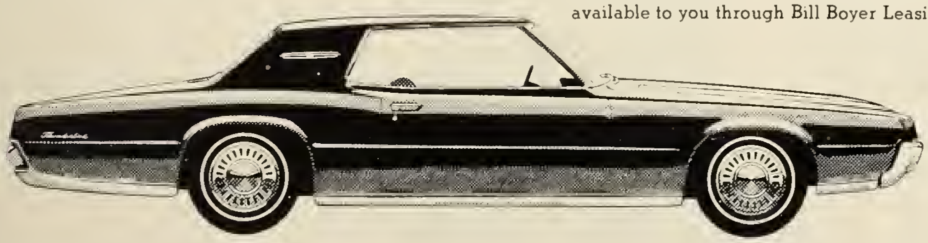

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(Continued from page 18A)

Some of the controversial questions in regard to etiology are not explored fully, and this is probably all to the good. Pathological illustrations are numerous and appropriate to the subject at hand. Some clinical conditions, such as the carpal tunnel syndrome, are probably not covered sufficiently. There are 132 illustrations that are for the most part of high quality, particularly the microphotographs.

In summary, this book serves a great need in providing the clinician with immediate reference source for a practical evaluation of peripheral vascular problems.

ROBERT D. STORY, M.D.
Fargo

Correlative Neurosciences: Part A, Fundamental Mechanisms (Progress in Brain Research, Vol. 21A)

by T. TOKIZANE *and* J. P. SCHADE, *363 pp., ill., American Elsevier Publishing Company, Inc., New York, 1966. $21*

This volume is the first of a group of 2, and it is devoted to articles of multidisciplinary nature by Japanese authors. The fact that the list of contributors is restricted to Japanese investigators cannot be inferred by the title or substitle and this may be misleading. The preface, however, makes it clear that this volume "particularly reflects the progress of Japanese research in the basic and clinical neurological sciences" and that the editors "trust this volume will provide a means of evaluating the level of brain research in Japan." This would be worthwhile in itself because although most Japanese scientists write at least some of their articles in English or in German, there is a certain number of them who have published only in Japanese and whose work is definitely worth knowing by the many Western investigators who do not know this language.

Most editions of symposia on restricted topics are very heterogeneous in subjects as well as in quality. This volume, dealing with a great variety of themes which are not guided by the relative unity of goals found in symposia, is necessarily even more multiform but the fact that apparently all the translations were done by the same individual or group of individuals gives the book a uniformity of style which makes pleasant reading and facilitates the correlation of some of the chapters that deal with similar subjects. All the illustrations are of high quality and are, for the most part, very enlightening.

The book comprises 14 chapters on basic neurosciences. For the purpose of this review, they may be classified in 6 sections: (1) neurophysiology (7 chapters), (2) neuroanatomy (2 chapters), (3) neurochemistry (2 chapters), (4) neuroendocrinology (1 chapter), (5) electronmicroscopic studies of synapses (1 chapter), and (6) histochemistry of the brain (1 chapter). There is a very complete author index, including all the names of junior authors corresponding to references cited and a subject index which is also of great value.

Since it would be impossible to cover in detail each chapter in a brief review, only the highlights, as they

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appear to the biased judgment of the reviewer, will be considered in some detail while the less important contributions will be only briefly mentioned.

The first chapter, on the septo-preoptico-hypothalamic system and its autonomic function contains 44 pages of useful information derived largely from previously published work of the author, Tadayasu Ban, and from the works of other Japanese. For somebody who does not specialize in these structures, it is difficult to conceive the universal influence that they have over all the bodily organs. The results of stimulation and destruction of different parts of the septo-hypothalamic system are described without giving experimental details and in the form of a review. The references, which fill 4 pages, include almost exclusively Japanese names.

The second chapter, by Taro Furukawa, describes experiments by the author and collaborators on the Mauthner cell of the goldfish. This is a useful model for synaptic physiology and the chapter contains useful details of technique for those who would be interested in reproducing some of this work. The references contain outstanding names among synaptologists in Japan and the world.

The third chapter, by Jasuji Katsuki, deals with hearing mechanisms in cats and monkeys and analyzes the functional organization of neurons at the different anatomic levels and the effects of efferent and nonefferent inhibition. The "funneling" mechanism in the auditory tract is discussed.

The chapter by Hiroshi Kumagay and collaborators about relationship between activity of the respiratory center and the EEG is of lower quality than most others. The same can be said about the next article, by Masanori Kurokawa and collaborators, dealing with metabolic studies on a special strain of mice with convulsive predisposition.

The chapter on morphological study of dendrite arborization in the brain stem, by Hajime Mannen, describes an original, ingenious, and useful method of microphotography and photogrammetry which permits the measurement of volume of neurons and the study of their dendritic arborizations in precise detail. As presented by the author, it is a very tedious and time consuming method but has all the characteristics to make it suitable for computer processing. If computer techniques were applied to this type of work, the results could be of much greater importance.

Central mechanisms of vision are studied by Koiti Motokawa and Hisao Suzuki in the 7th chapter. This is a study with microelectrodes with its inherent difficulties and shortcomings. Not much new is added. The following chapter on excitation and inhibition in thalamic neurons after cutaneous input deprivation is also a neurophysiologic study of single units with interesting results. Two more chapters on neurophysiology include a correlation of behavior and frequency analysis of EEG using good instrumentation but with doubtful results, and the influence of synchronization and desynchronization on thalamic and cortical neurons.

Shimizu and Abe present some interesting new data on histochemical studies of glucose metabolism in the brain, and amino acid metabolism is discussed by Yasuzo Tsukada who correlates these substances with different behavioral situations. These correlations are of questionable validity.

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(Continued on page 25A)

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News Briefs . . .

North Dakota

DR. ANTONIO R. RILLO has joined the staff of the Red River Valley Clinic in Wahpeton and will operate the Fairmount Clinic in Fairmount. Dr. Rillo had been on the St. Luke's hospital staff in Fargo after leaving practice in the Philippines, where he graduated in 1954.

* * * *

DR. EUSEBIO R. MENDOZA, an internist, has joined Drs. Gordon and Jane Magill in practice in the Medical Arts Building, Fargo. Dr. Mendoza, a native of the Philippines, was executive assistant to the Philippine Secretary of Health before joining the staff of St. Luke's Hospital in Fargo in 1965.

* * * *

DR. DEMOS HILIO, a native of Greece, has joined the staff at the Crosby Clinic, Crosby. Dr. Hilio practiced for a short time in Westhope.

* * * *

DR. W. A. PINSONNEAULT has closed his practice in Drayton and joined the staff of the Dilmore Clinic Medical Group in Roseau, Minn.

Minnesota

DR. BRUICE AMUNDSON and family of Halstad have arrived in Monrovia, Liberia, Africa, where Dr. Amundson will serve for two years as a staff doctor with Peace Corps Volunteers.

* * * *

ST. GABRIEL'S HOSPITAL in Little Falls has installed a dialysis unit, the first in the state north of the Twin Cities.

* * * *

DR. GLENN N. BURGESS, director of training at the Anoka State Hospital, has joined the staff of the Northern Pines Mental Health Center in Little Falls as a psychiatric consultant.

* * * *

DR. LAWRENCE J. LEONARD was honored by the Minnesota Medical Association for fifty years of practice in the Minneapolis area.

* * * *

DR. JOHN T. GOSWITZ, a general surgeon, has resigned his position at the Mankato Clinic to accept a position with a medical group in Manitowoc, Wis.

* * * *

DR. O. J. SWENSON was honored with an open house for his forty years of practice in Waseca.

* * * *

DR. EDMUND BURKE, a Mayo Clinic pediatrician, has been elected president of the Southern Minnesota Medical Association. Other officers include Dr. John Eustermann of Mankato, first vice-president, and Dr. Robert Conley of Mankato, secretary-treasurer.

* * * *

DR. MUSTAFA VIDINLI, a native of Ankara, Turkey, has joined the staff of the Delmore Clinic in Roseau.

* * * *

DR. EDITH PARKHILL, a member of Mayo Clinic's surgical pathology section since 1937, has retired from the Clinic.

DR. VIKTOR WILSON, Rochester-Olmsted County public health officer, received the Albert J. Chesley Memorial Award at the annual meeting of the Minnesota Public Health Association. Dr. Malcolm Hargraves of Rochester received the Harvey G. Rogers Award for his work in preservation of state water resources as chairman of the Minnesota Water Pollution Control Commission.

* * * *

DR. JESSE E. EDWARDS, professor of pathology at the University of Minnesota and director of laboratories at the Charles T. Miller Hospital, St. Paul, has been named president-elect of the American Heart Association.

* * * *

DR. DONALD E. STEWART, a Crookston (Minn.) surgeon, has been reelected president of the American Cancer Society's Minnesota Division.

* * * *

DR. B. J. KENNEDY, associate medical professor at the University of Minnesota, has been reelected director-at-large of the American Cancer Society.

* * * *

DR. GEORGE B. LOGAN, professor of pediatrics at the Mayo Graduate School of Medicine, has been named vice-president and president-elect of the American Academy of Pediatrics.

* * * *

DR. C. ALLEN GOOD, head of the section of diagnostic roentgenology of the Mayo Clinic and professor of radiology in the Mayo Graduate School, has been named president-elect of the American Roentgen Ray Society.

* * * *

THE NATIONAL METHODIST CONVOCATION on medicine and theology will be held in Rochester, April 5 to 7, 1967. The program is sponsored by The Council of Bishops and Board of Hospitals and Homes, Board of Christian Social Concerns, National Division of the Board of Missions, and Commission on Chaplains in cooperation with the Rochester Methodist Hospital and the Mayo Clinic.

* * * *

THE MAYO CLINIC has appointed 8 new staff physicians and the Mayo Graduate School of Medicine has appointed 16 assistant professors and instructors. The staff appointments are Dr. David Ahmann, a graduate of Marquette University; Dr. Robert Sawtell, a graduate of the University of Nebraska; Dr. Lloyd Wood, a graduate of the University of Minnesota; Dr. Van Lawrence, a graduate of the University of Minnesota; Dr. David Williams, a graduate of New York Medical College; Dr. James Frantam, a graduate from the Chicago College of Chiropody; Dr. Aidan Carney, a graduate of the University College in Dublin, and Dr. George Farrow, a graduate of Louisiana State University. Five new assistants to the staff are Drs. William Douglas, James Garber, and John Wyman, all internal medicine, James Becton, orthopedic surgery, and Sidney Maurer, pediatrics. Dr. Joaquin Aldrete was appointed a chief resident in surgery. Appointed assistant professors at the Graduate School are Drs. Paul Didisheim, Kai Rehder, and Wiley Sams. New appointees to the rank of instructor are Drs. William Baldus, Gene Hunder, Carlo Veneziale, Colum Gorman, Alan Sessler, Dan Tolman, Andrew Engel, Albert Rhoton, Jr., Donald Ritter, John Simons, Clyde Culp, Robert Lee, and Glen Duncan.

(Continued on page 24A)

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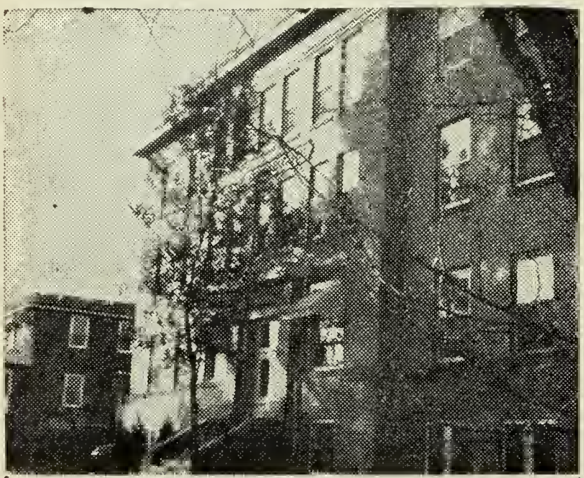

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NEWS BRIEFS

(Continued from page 23A)

South Dakota

DR. JOHN L. CALENE of Aberdeen was honored by the South Dakota region College of Physicians for being the first internist and first member of the College of Physicians in the state.

* * * *

DR. REUBEN BAREIS of Rapid City has been elected president of the South Dakota Society of Internal Medicine. Other officers include Dr. H. Street Shinning of Rapid City, secretary-treasurer; Dr. Clark F. Johnson of Yankton, president-elect, and Dr. Warren Jones of Sioux Falls, trustee.

* * * *

DR. PETER KRYGER has closed his practice in Groton to establish a new office in Deadwood.

Deaths . . .

DR. JOSEPH F. BICEK, 67, St. Paul physician and surgeon and former instructor at the University of Minnesota, died Sept. 27 of head injuries suffered in a fall. Dr. Bicek was a 1921 honor graduate of the University of Minnesota Medical School.

* * * *

DR. RUDOLPH C. LOGEFEIL, 72, of Edina died Oct. 16. Dr. Logefeil, a graduate of the University of Minnesota, was a former chief of staff at Fairview Hospital and medical director of the Evangelical Alliance Mission.

* * * *

DR. WILLIAM F. MENOLD, 52, a St. Paul obstetrician and gynecologist, died Oct. 17. Dr. Menold was a graduate of the University of Minnesota Medical School.

* * * *

DR. GEORGE SCHMIDT, 85, of Minneapolis died Oct. 7. Dr. Schmidt, physician and surgeon and graduate of the Minneapolis College of Physicians and Surgeons, had retired from practice in 1960.

* * * *

DR. F. E. ANDERSON, 66, who had practiced medicine in Underwood, N. Dak., for thirty-five years, died Oct. 8. A graduate of the University of Minnesota, he had served as McLean County coroner and first district health officer.

* * * *

DR. OREN L. KIRKLIN, 63, a former Mayo Clinic physician, died Sept. 2 in Indianapolis, Ind., where he had practiced since 1947.

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(Continued from page 21A)

of synapses in the earthworm, crayfish, and squid—including a series of very impressive electron microphotographs of excellent technical quality.

The one purely neuroanatomic chapter by Toshio Kusama and collaborators describes the projections of motor, somatic sensory, and auditory and visual cortices in cats as studied with classical techniques but with new staining methods.

In summary, this book contains a very large amount of information, most of it useful. It should be a valuable addition to the libraries of scientists interested in basic neurological problems, including all those in academic or research positions. For the practitioner, on the other hand, it would probably not be worth as much since most of the book's contents has no direct application to medical problems, and its price, while justified by the quality of the edition, is rather high.

FERNANDO TORRES, M.D.
Minneapolis

Data Acquisition and Processing in Biology and Medicine, Volume 4: Proceedings of the 1964 Rochester Conference

edited by KURT ENSLEIN *with* JOHN F. KINSLOW, *252 pp., ill., Pergamon Press, New York City, 1966. $14.50*

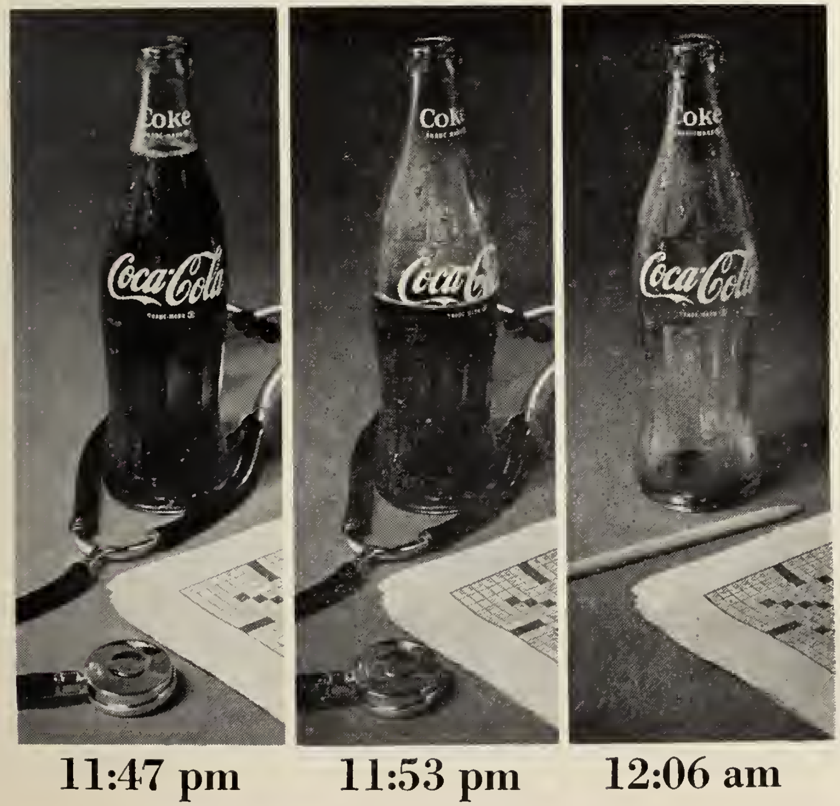
The fourth in a series of reported conferences, this volume describes many separate projects covering a wide range of interests in biology, medicine, and electronics. Because of the variety of subjects covered—each with highly specialized techniques—the book is of questionable value to a physician.

The four-volume set should be available in any hospital or medical school library. The primary value of this type of text is that it provides us with a general description of the frontiers of acquisition of medical data.

Several projects reported here deal with the processing of multiple analog signals derived from human or animal subjects. They include: physiological data acquisition and processing for a stress-in-learning study, computer-oriented study of human metabolism, acquisition and processing of fetal cardiac data: electrical axis of the fetal heart, observation of fetal heart rate during cesarean section, cortical auditory response in human beings, and information processing by electric fishes.

A special characteristic of this volume is the emphasis on storage of information and retrieval applications in biology and medicine. The very multiplicity of effort and the apparent success of some of these developmental projects can predict the future for medical documentation and medical research files. Much is being done and more could be accomplished if the general medical community were aware of the potential. In this respect, the authors have included the following project reports: computer-based colony records system for the Oregon Regional Primate Research Center, retrieving and processing medical measurement data, retrieval system for Eastman-Kodak Company mortality experience, data manipulation in investigational new drug applications, computerization of a pharmaceutical manufacturer, study of a medical documentation center of medium size: 12,000 records per year, objective content analysis of

(Continued on page 26A)



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(Continued from page 25A)

psychotherapy by computer, methods of microglossary analysis, and mechanized image systems.

In summary, the book presents a selection of project reports, all with heavy emphasis on data acquisition. The book is not unique in this regard, nor is it one of the best. Individuals specializing in measurement and data acquisition may wish a personal copy. The physician would find the four-volume set a useful library aid when used in conjunction with similar published material.

EUGENE A. JOHNSON, PH.D.
Minneapolis

Congenital Clubfoot

by EMIL D. W. HAUSER, M.D., *94 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $5.75*

This monograph was written by a man with extensive personal experience in the treatment of talipes equinovalgus. The author stresses [1] early diagnosis, [2] early conservative treatment, and [3] his personal technique of conservative management by cohesive bandages.

The first three sections of the book dealing with the etiology, pathology, and diagnosis of clubfoot are excellent and reflect the author's extensive bibliography. However, after reading and then rereading the author's description of a technique for conservative treatment, I felt I would need personal instruction from the author to master the method.

This is not intended as a "how to" book, except for the section on the technique of bandaging. The author's preferance for subcutaneous lengthening of Achilles tendon is not held by the reviewer or most orthopedists at this time. His mention of the Thomas wrench for late or neglected cases may lead the unwary into the impression that this method is still in use. In the normal course of orthopedics today, one is unable to find a Thomas wrench in the hospital instrument cabinet.

I believe this book would be of interest to those treating clubfeet. The review of general principles is excellent, but the material regarding diagnosis and early treatment is well emphasized elsewhere in the literature.

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NEW BOOKS RECEIVED

Health and Humanity: An Introduction to Medicine
by JOHN W. TODD, 246 pp., Pergamon Press, New York City, 1966. $4.50

Psychopathic Disorders
edited by MICHAEL CRAFT, M.D., 234 pp., ill., Pergamon Press, New York City, 1966. $4.50

Carotid-Cavernous Fistula
by WALLACE B. HAMBY, M.D., 139 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $7.50

Recent Advances in Nuclear Medicine: Based on a Symposium Sponsored by the Department of Radiology of the Hahnemann Medical College
edited by MILLARD N. CROLL, M.D., and LUTHER W. BRADY, M.D., 260 pp., ill., Appleton-Century-Crofts, New York, 1966. $12.50

Atlas of Hernia Repair
by CARL H. CALMAN, M.D., 159 pp., ill., C. V. Mosby Co., St. Louis, 1966. $16.75

Endocrine Surgery in Human Cancers
by PAUL JURET, M.D., 2d. ed., (translated from original French by Ranes Chakravorty and Ernest Greenbert), 412 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $15.50

Aspects of Comparative Ophthalmology: Proceedings of a Symposium organized by The British Small Animal Veterinary Association, 1965
edited by OLIVER GRAHAM-JONES, 341 pp., ill., Pergamon Press, New York, 1966. $13

The Spontaneous Regression of Cancer
by WILLIAM BOYD, M.D., 99 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $5.75

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NEW BOOKS RECEIVED

Hypochondriacal Syndromes
by G. A. LADEE, 424 pp., American Elsevier Publishing Co., Inc., New York, 1966. $21.50

Clinical Examination of the Jugular Venous Pulse
by ARNOLD L. COLMAN, M.D., 183 pp., ill., Charles C Thomas, Springfield, Ill., 1966. $10.50

Differential Diagnosis of Congenital Heart Disease: A Roentgenographic, Electrocardiographic and Phonocardiographic Treatise
by NIKOLAUS SCHAD, M.D., RALPH KUNZLER, M.D., and TEOMAN ONAT, M.D., 454 pp., ill., Grune & Stratton, New York, 1966. $29.75

The Ocular Fundus in Neurologic Disease: A Diagnostic Manual and Stereo Atlas
by WILLIAM FLETCHER HOYT, M.D. and DIANE BEESTON, A.B., 128 pp., ill., C. V. Mosby Co., St. Louis, 1966. $35

Stereoscopic Atlas of Mastoidotympanoplastic Surgery
by HAROLD F. SCHUKNECHT, M.D., WERNER D. CHASIN, M.D., and JOHN M. KURKJIAN, M.D., 92 pp., ill., C. V. Mosby Co., St. Louis, 1966. $26.50

Questions and Answers in Orthopaedics: For Students, Interns, Residents, and Board Aspirants
by FLOYD G. GOODMAN, M.D. and GEORGE R. SCHOEDINGER III, M.D., 244 pp., C. V. Mosby Co., St. Louis, 1966. $9.85

Behavior Therapy Techniques: A Guide to the Treatment of Neuroses (The Commonwealth and International Library of Science Technology Engineering and Liberal Studies)
by JOSEPH WOLPE, M.D. and ARNOLD A. LAZARUS, Ph.D., 198 pp., ill., Pergamon Press, New York, 1966. $2.75

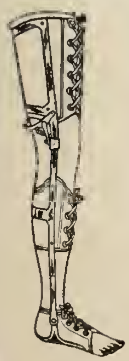
Biological Treatment of Mental Illness: Proceedings of the II International Conference of the Manfred Sakel Foundation, Held Oct. 31 to Nov. 3, 1962, at the New York Academy of Medicine, New York
edited by MAX RINKEL, M.D., 1025 pp., ill., Farrar, Straus and Giroux, New York, 1966. $25

Alphabetical Index of Roentgen Diagnoses and Procedures with Code Numbers of the American College of Radiology
by GERHART S. SCHWARZ, M.D. and HENRY J. POWSNER, M.D., 230 pp., Charles C Thomas, Springfield, Ill., 1966. $8.50

Synopsis of Dermatology
by WM. D. STEWART, M.D., JULIUS L. DANTO, M.D., and STUART MADDIN, M.D., 664 pp., ill., C. V. Mosby Co., St. Louis, Mo., 1966. $10.85

The Heart and Circulation in the Newborn and Infant
edited by DONALD E. CASSELS, M.D., 426 pp., ill., Grune & Stratton, New York, 1966. $9.50

International Encyclopedia of Pharmacology and Therapeutics, Section 12: Ganglionic Blocking and Stimulating Agents: Muscarinic and Nicotinic Stimulant Actions of Autonomic Ganglia
by R. L. VOLLE, 110 pp., ill., Pergamon Press, New York, 1966. $5



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GENERAL PRACTITIONER WANTED—To associate with solo practitioner currently doing over $100 M annual volume. Guaranteed minimum salary, plus bonus. Central Minnesota Lake Region. Write Box 43 Journal-Lancet.

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GENERAL PRACTITIONER, associate, wanted. Small town, Minnesota near Fargo-Moorhead. Previous partnership, modern hospital, 12 miles on four lane highway. Resort area, good hunting, fishing, skiing. Good school and churches. Salary and partnership open. Call or write A. S. Midthune, M.D., telephone 238-5941 area code 218, Lake Park, Minn.

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EFFECTIVE in clinical study of 55 cases[1,2] with varied severity and extent of involvement. Marked clinical improvement was noted within 5-7 days in 90%; proctologic improvement in 94% within 3 weeks. **CORTENEMA** provides both topical and systemic effects because Hydrocortisone Alcohol is absorbed to a significant extent from the colon.

CONVENIENT for both hospital and out-patient use. The standardized, disposable single-dose unit is ready to use, requires no mixing and is simply self-administered.

ECONOMICAL since the average dosage requires only one enema daily for 2 or 3 weeks, then one every other day until remission is established. The selection of Hydrocortisone permits lower patient cost without sacrificing efficacy.

1 Sherman, L. F. Minnesota Med 48,605 May, 1965. 2 Sherman, L. F. Personal Communication.

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Each 60 cc. unit contains:

Hydrocortisone..100 mg. in aqueous, isotonic saline containing methylcellulose as a suspending agent and emollient, polysorbate 80, and 0.18% methylparaben and 0.02% propylparaben, as preservatives.

Description: CORTENEMA Hydrocortisone Retention Enema is a completely disposable, single-dose unit consisting of a flexible plastic container with a lubricated applicator tip for rectal administration. It is designed to permit self-administration and, therefore, it is suitable for both out-patient and hospital use. It also may be diluted with isotonic saline for administration by intrarectal drip.

CORTENEMA consists of a suspension of partially solubilized hydrocortisone alcohol in an aqueous vehicle. Thus, it provides the potent anti-inflammatory effect characteristic of the corticosteroids. Because hydrocortisone alcohol is absorbed to some extent from the colon, CORTENEMA provides both topical and systemic actions.

Indications: CORTENEMA Hydrocortisone Retention Enema is indicated as an adjunct in the treatment of idiopathic nonspecific ulcerative colitis. It is most useful in cases involving the rectum, sigmoid and left colon, where it exerts a topical effect. Due to its systemic action, CORTENEMA has proved effective in certain cases extending to the transverse and ascending colons.

Rectal steroid therapy brings about prompt symptomatic and proctologic remissions in a significant proportion of patients, but it apparently does not alter the recurrent and progressive nature of ulcerative colitis. Therefore, this form of treatment is not recommended for prophylaxis during periods of remission.

Contraindications: Local contraindications to the use of intrarectal steroids include obstruction, abscess, perforation, peritonitis, fresh intestinal anastomoses, extensive fistulas and sinus tracts. Tuberculosis (active, latent or questionably healed), ocular herpes simplex, and acute psychosis are usually considered absolute contraindications to the use of corticosteroids.

Relative contraindications include active peptic ulcer, acute glomerulonephritis, myasthenia gravis, osteoporosis, diverticulitis, thrombophlebitis, psychic disturbances, pregnancy, diabetes, hyperthyroidism, acute coronary disease, hypertension, limited cardiac reserve, and local or systemic infections, including fungal or exanthematous diseases. Where these conditions exist, the expected benefits from CORTENEMA must be weighed against the risks involved in its use.

If clinical or proctologic improvement does not occur within two or three weeks after starting CORTENEMA, discontinue its use.

Precautions: CORTENEMA Hydrocortisone Retention Enema should be administered with caution in patients with severe ulcerative disease because these patients are predisposed to perforation of the bowel wall. In the advanced stages of chronic ulcerative colitis, where there is loss of mucosa, and thickening and fibrosis of the bowel wall, steroid therapy theoretically might hasten deterioration, although this has not been proved with steroids in actual practice.

In severe cases, where surgery is imminent in the absence of marked clinical improvement, it is hazardous to wait more than a few days for a satisfactory response to medical treatment.

Because of the possibility of adrenal insufficiency caused by suppression of the adrenal cortex by glucocorticoids especially after prolonged therapy, it is important that therapy be withdrawn gradually. If the patient is subjected to unusual stress, while on therapy or up to a year after discontinuation of steroids, adequate supportive measures and increased or reinstated systemic steroid therapy are indicated. In the case of surgery, these measures should be continued throughout the pre- and postoperative recovery periods, bearing in mind the possible deleterious effects of corticosteroids on fresh intestinal anastomoses.

Steroid therapy might impair prognosis in surgery by increasing the hazard of infection. If infection is suspected, appropriate antibiotic therapy must be administered, usually in larger than ordinary doses.

General precautions common to all corticosteroid therapy should be observed during treatment with CORTENEMA, including those pertaining to growth suppression in children during prolonged use. Patients should be kept under close observation. If severe reactions or idiosyncrasies occur, steroids should be discontinued immediately and appropriate measures instituted.

If it is necessary to use CORTENEMA in pregnant patients, their infants should be closely observed for signs of hypoadrenalism; and appropriate measures, including administration of corticosteroids, should be instituted if such signs are seen.

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FOR RECTAL USE ONLY

Adverse Reactions: CORTENEMA Hydrocortisone Retention Enema may produce all of the side effects known to occur with other forms of hydrocortisone therapy. These include moon face, buffalo hump, fluid retention, excessive appetite and weight gain, abnormal fat deposits, mental symptoms, hypertrichosis, acne, striae, ecchymosis, increased sweating, pigmentation, dry scaly skin, thinning scalp hair, thrombophlebitis, decreased resistance to infection, negative nitrogen balance with delayed bone and wound healing, menstrual disorders, neuropathy, peptic ulcer, decreased glucose tolerance, hypopotassemia, adrenal insufficiency, necrotizing angiitis, hypertension, pancreatitis and increased intraocular pressure.

In children, suppression of growth may occur. Increased intracranial pressure may occur and possibly account for headache, insomnia and fatigue. Subcapsular cataracts may result from prolonged usage. Long-term use of all corticosteroids results in catabolic effects characterized by negative protein and calcium balance. Osteoporosis, spontaneous fractures and aseptic necrosis of the hip and humerus may occur as part of this catabolic phenomenon.

Where hypopotassemia and the other symptoms associated with fluid and electrolyte imbalance call for potassium supplementation and salt-poor or salt-free diets, these may be instituted and are compatible with the diet requirements for ulcerative colitis.

Dosage and Administration: The use of CORTENEMA Hydrocortisone Retention Enema as an adjunct in the treatment of ulcerative colitis is predicated upon the concomitant use of modern supportive measures, such as blood replacement, rational dietary control, antispasmodics and sedatives, antibacterial therapy, and systemic steroids.

The usual dose is one CORTENEMA Hydrocortisone Retention Enema daily for two or three weeks and every second day thereafter, administered intrarectally in the evening before retiring. Every effort should be made to retain the medication for at least one hour, preferably all night. This may be facilitated by prior sedation and or antidiarrheal medication. If clinical or proctologic improvement fail to occur within two or three weeks, discontinue the drug.

For administration by retention enema, instruct the patient to lie on his left side during instillation. Shake the bottle vigorously to resuspend the insoluble portion of hydrocortisone. Expose the lubricated tip by removal of the protective sheath, grasping the bottle at the neck where it is most rigid. Carefully insert the lubricated tip into the rectum in the direction of the sacrum. Slowly express the contents by compressing the container. After instillation, the patient should remain on his left side for at least 30 minutes, to allow distribution of the medication throughout the descending colon and rectum.

For coverage of more distant segments of the colon, CORTENEMA Hydrocortisone Retention Enema may be diluted to from 100 cc. to 300 cc. with isotonic saline and administered by intrarectal drip.

The duration of treatment is dependent on the degree of response. If a satisfactory response is to be obtained, it usually occurs within five to seven days, as evidenced by a marked reduction of clinical symptoms. Improvement in the appearance of the mucosa, gauged by barium enemas and sigmoidoscopic examinations, may lag somewhat behind clinical improvement. The usual duration of therapy is two weeks, although some cases require therapy for longer periods (up to two or three months). Minimal control of symptoms is an insufficient basis for the prolonged use of CORTENEMA. If there is no clinical or proctologic response within two or three weeks, or if the patient's condition worsens, discontinue the drug.

Because of hydrocortisone absorption, proper precautions against unwanted systemic reactions or side effects should be observed. Symptomatic improvement, evidenced by decreased diarrhea, weight gain, improved appetite, lessened fever, and decrease in leukocytosis, may be misleading and should not be used as the sole criterion in judging efficacy. Actual sigmoidoscopic examination and X-ray visualization are most reliable. Since steroids can inhibit wound healing, enema or drip therapy should not be employed in the immediate or early postoperative period following ileorectostomy.

How Supplied: CORTENEMA Hydrocortisone Retention Enema is supplied in boxes of seven single-dose units.

Caution: Federal law prohibits dispensing without a prescription.

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Each teaspoon (5 ml.) contains codeine phosphate 5 mg.,
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congestion
running nose
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bright red, pleasant-tasting, raspberry-flavored syrup

Pediacof is different. It is designed especially for children, and each ingredient is in the right proportion. The potassium iodide in Pediacof is so well masked that it is virtually unnoticeable. Children like the sweet raspberry flavor of bright red Pediacof.

Dosage: Children from 6 months to 1 year, ¼ teaspoon; from 1 to 3 years, ½ to 1 teaspoon; from 3 to 6 years, 1 to 2 teaspoons; and from 6 to 12 years, 2 teaspoons. These doses are to be given every four to six hours as needed.

How supplied: Bottles of 16 fl. oz.

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Exempt Narcotic.

Side effects: The only significant untoward effects that have occurred are mild anorexia and an occasional tendency to constipation. However, discontinuance of Pediacof has seldom been required. Mild drowsiness occurs in some patients but, when cough is relieved, the quieting effect of Pediacof is considered beneficial in many instances.

Precautions and contraindications: Patients with tuberculosis or those who are known to be sensitive to iodides should not be given Pediacof.

Caution should be exercised if Pediacof is administered to patients with cardiac disorders, hypertension or hyperthyroidism.

Warning: May be habit forming.

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